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|--|--|---|--|--|--|
| FORM PTO-1390<br>(REV 11-98)   |  | U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE     |  | ATTORNEYS DOCKET NUMBER: Heska USNP  |  |
| <b>TRANSMITTAL LETTER TO THE UNITED STATES<br/>DESIGNATED/ELECTED OFFICE (DO/EO/US)<br/>CONCERNING A FILING UNDER 35 U.S.C. 371</b>  |  |   |  | US APPLICATION NO. (If known, see 37 CFR 1.5)<br>09/408, 584<br><br><div style="text-align: center; font-size: 1.2em;">10/090224</div> |  |
| INTERNATIONAL APPLICATION NO.<br>PCT/US00/26870  |  | INTERNATIONAL FILING DATE<br>29 September 2000 (29.09.2000) |  | PRIORITY DATE CLAIMED<br>29 September 1999 (29.09.1999)  |  |
| TITLE OF INVENTION<br><br>INTRANASAL DELIVERY SYSTEM   |  |   |  |  |  |
| APPLICANT(S) FOR DO/EO/US<br><br>HESKA CORPORATION   |  |   |  |  |  |
| Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:  |  |   |  |  |  |
| <ol style="list-style-type: none"> <li>1. <input checked="" type="checkbox"/> This is the <b>FIRST</b> submission of items concerning a filing under 35 U.S.C. 371.</li> <li>2. <input type="checkbox"/> This is the <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a filing under 35 U.S.C. 371.</li> <li>3. <input type="checkbox"/> This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b)) and PCT articles 22 and 39(1).</li> <li>4. <input checked="" type="checkbox"/> A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.</li> <li>5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2))               <ol style="list-style-type: none"> <li>a. <input checked="" type="checkbox"/> is transmitted herewith (required only if not transmitted by the International Bureau).</li> <li>b. <input type="checkbox"/> has been transmitted by the International Bureau.</li> <li>c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).</li> </ol> </li> <li>6. <input type="checkbox"/> A translation of the International Application into English (35 U.S.C. 371(c)(2)).</li> <li>7. <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)).               <ol style="list-style-type: none"> <li>a. <input type="checkbox"/> are transmitted herewith (required only if not transmitted by the International Bureau).</li> <li>b. <input type="checkbox"/> have been transmitted by the International Bureau.</li> <li>c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.</li> <li>d. <input checked="" type="checkbox"/> have not been made and will not be made.</li> </ol> </li> <li>8. <input type="checkbox"/> A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).</li> <li>9. <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).</li> <li>10. <input type="checkbox"/> A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).</li> </ol> |  |   |  |  |  |
| <b>Items 11. to 16. below concern document(s) or information included:</b>   |  |   |  |  |  |
| <ol style="list-style-type: none"> <li>11. <input checked="" type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98.</li> <li>12. <input checked="" type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.</li> <li>13. <input checked="" type="checkbox"/> A FIRST preliminary amendment.<br/> <input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment.</li> <li>14. <input type="checkbox"/> A substitute specification.</li> <li>15. <input type="checkbox"/> A change of power of attorney and or address letter.</li> <li>16. <input checked="" type="checkbox"/> Other items or information: Application Data Sheet, Power of Attorney, Express Mail Certificates, firm Letter of Transmittal, and a return receipt postcard</li> </ol>   |  |   |  |  |  |

|  |              |  |           |  |          |
|--|--------------|--|-----------|--|----------|
| U.S. APPLICATION NO. (If known, see 37 CFR 1.5<br>09/408,584 <b>10/089224</b>  |              | INTERNATIONAL APPLICATION NO<br>PCT/US00/26870 |           | ATTORNEY'S DOCKET NUMBER<br>Heska UNSP |          |
| 17. ■ The following fees are submitted:<br><b>BASIC NATIONAL FEE (37 CFR 1.492(a) (1) - (5):</b><br>Neither international preliminary examination fee (37 CFR 1.482)<br>nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO<br>and International Search Report not prepared by the EPO or JPO. . . . . \$1000.00<br><br>International preliminary examination fee (37 CFR 1.482) not paid to<br>USPTO but International Search Report prepared by the EPO or JPO. . . . . \$860.00<br><br>International preliminary examination fee (37 CFR 1.482) not paid to<br>USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO. . . \$710.00<br><br>International preliminary examination fee paid to USPTO (37 CFR 1.482)<br>but all claims did not satisfy provisions of PCT Article 33(1)-(4). . . . . \$690.00<br><br>International preliminary examination fee paid to USPTO (37 CFR 1.482)<br>and all claims satisfy provisions of PCT Article 33(1)-(4). . . . . \$100.00<br><br><b>ENTER APPROPRIATE BASIC FEE AMOUNT =</b> |              |  |           | <b>CALCULATIONS (PTO USE ONLY)</b>     |          |
|  |              |  |           |  |          |
| Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30<br>months from the earliest claimed priority date (37 CFR 1.492(e)).   |              |  |           | \$                                     |          |
| CLAIMS   | NUMBER FILED | NUMBER EXTRA                                   | RATE      |  |          |
| Total claims   | 158 - 20 =   | 138  | X \$18.00 | \$ 2484.00                             |          |
| Independent claims   | 10 - 3 =     | 7  | X \$80.00 | \$ 560.00                              |          |
| MULTIPLE DEPENDENT CLAIM(S) (if applicable)  |              |  | +\$270.00 | \$ -0-                                 |          |
| <b>TOTAL OF ABOVE CALCULATIONS =</b>   |              |  |           | <b>\$ 3144.00</b>                      |          |
| Reduction of 1/2 for filing by small entity, if applicable. A Small Entity Statement<br>must also be filed (Note 37 CFR 1.9, 1.27, 1.28).  |              |  |           | \$ 1572.00                             |          |
| <b>SUBTOTAL =</b>  |              |  |           | <b>\$ 1572.00</b>                      |          |
| Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30<br>months from the earliest claimed priority date (37 CFR 1.492(f)).  |              |  |           | +                                      | \$ -0-   |
| <b>TOTAL NATIONAL FEE =</b>  |              |  |           | <b>\$ 1572.00</b>                      |          |
| Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be<br>accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property  |              |  |           | +                                      | \$ 40.00 |
| <b>TOTAL FEES ENCLOSED =</b>   |              |  |           | <b>\$ 1612.00</b>                      |          |
| Amount to be:  |              |  |           | Refunded                               | \$       |
| Amount to be:  |              |  |           | Charged                                | \$       |

10/089224  
JC13 Rec'd PCT/PAL 27 MAR 2002

Express Mail No: EL913299804US

Attorney Docket: Heska USNP

IN THE UNITED STATES PATENT  
AND TRADEMARK OFFICE

In Re the National Phase Application of: Heska Corporation

Serial Number: (original) US 09/408,584 New: \_\_\_\_\_  
(PCT) PCT/US00/26870

Filed: (original US) 29 September 1999 New: \_\_\_\_\_  
(PCT) 29 September 2000

For: Intranasal Delivery System

CERTIFICATE OF EXPRESS MAILING

I, Barbara Graves, hereby certify to the truth of the following items:

1. I am an employee of Santangelo Law Offices, P.C., 125 South Howes, 3rd Floor, Fort Collins, Colorado 80521.
2. I have this day deposited the attached Declaration for Patent Application of Steven J. Penner and Randal W. Sebring with the United States Postal Service as "Express Mail" for mailing to the Assistant Commissioner of Patents, BOX PCT, Washington, D.C. 20231.

Dated this 27 day of March, 2002.

Barbara Graves

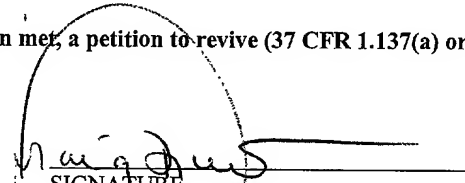
2002-03-27 14:26:00

- a. ☒ A check in the amount of **\$1612.00** to cover the above fees is enclosed.
- b. ☐ Please charge my Deposit Account No. \_\_\_\_\_ in the amount of \$ \_\_\_\_\_ to cover the above fees.
- c. ☐ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any over payment to Deposit Account No. \_\_\_\_\_. A Duplicate copy of this sheet is enclosed.

Note: Where the appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending process.

SEND ALL CORRESPONDENCE TO:

Santangelo Law Offices, P.C.  
125 South Howes, Third Floor  
Fort Collins, CO 80521

  
SIGNATURE  
CRAIG R. MILES  
NAME

45,954  
REGISTRATION NUMBER

20080327 14:26:00



Express Mail No: EL913299804US  
Attorney Docket: Heska USNP

IN THE UNITED STATES PATENT  
AND TRADEMARK OFFICE

In Re the National Phase Application of: Heska Corporation

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Filed: (original US) 29 September 1999 New: \_\_\_\_\_  
(PCT) 29 September 2000

For: Intranasal Delivery System

CERTIFICATE OF EXPRESS MAILING

I, Barbara Graves, hereby certify to the truth of the following items:

1. I am an employee of Santangelo Law Offices, P.C., 125 South Howes, 3rd Floor, Fort Collins, Colorado 80521.
2. I have this day deposited the attached Power of Attorney with the United States Postal Service as "Express Mail" for mailing to the Assistant Commissioner of Patents, BOX PCT, Washington, D.C. 20231.

Dated this 27 day of March, 2002.

Barbara Graves

20020327 1426300T

Express Mail No: EL913299804US  
Attorney Docket: Heska USNP

IN THE UNITED STATES PATENT  
AND TRADEMARK OFFICE

In Re the National Phase Application of: Heska Corporation

Serial Number: (original) US 09/408,584 New: \_\_\_\_\_  
(PCT) PCT/US00/26870

Filed: (original US) 29 September 1999 New: \_\_\_\_\_  
(PCT) 29 September 2000

For: Intranasal Delivery System

APPLICATION DATA SHEET

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### **Application Information**

Title Line One: Intranasal Delivery System  
Title Line Two:  
Total Drawing Sheets: Eleven (11)  
Formal Drawings: Yes  
Application Type: US National Phase  
Attorney Docket: Heska-USNP

### **Representative Information**

Attorney Name: Luke Santangelo, Esq.  
Registration No: 31,997  
Attorney Name: Craig R. Miles, Esq.  
Registration No: 45,954  
Attorney Name: Alfred K. Wiedmann Jr., Esq.  
Registration No: 48,033

### **Continuity Information**

This application is a: National Phase Application of  
Application One: PCT/US00/26870  
Filing Date: September 29, 2000  
which is also a: continuation of  
Application Two: 09/408,584  
Filing Date: September 29, 1999

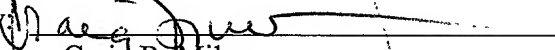
This application claims priority and the benefit of the above-identified applications.

### **Assignee Information**

Assignee Name: Heska Corporation  
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State or Province: Colorado  
Country: United States of America  
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Dated this 27 day of March, 2002.

Respectfully Submitted,  
SANTANGELO Law Offices, P.C.

By:   
Craig R. Miles  
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appldata.sheet

JG131332 PCT J 27 MAR 2002

Express Mail No: EL913299804US

Attorney Docket: Heska USNP

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IN THE UNITED STATES PATENT  
AND TRADEMARK OFFICE

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In Re the National Phase Application of: Heska Corporation

Serial Number: (original) US 09/408,584 New: \_\_\_\_\_  
(PCT) PCT/US00/26870

Filed: (original US) 29 September 1999 New: \_\_\_\_\_  
(PCT) 29 September 2000

For: Intranasal Delivery System

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**PRELIMINARY AMENDMENT**

This national stage application presents only claims for examination which have been indicated in the International Preliminary Examination Report prepared by the United States Patent and Trademark Office as satisfying the criteria of PCT Article 33(1)-(4) as to novelty, inventive step and industrial applicability. The applicant has amended the application only to the extent necessary to eliminate objections as to form or to cancel rejected claims. As such, the applicant has paid the fee as set forth in 37 C.F.R. §1.492(a)(4). The applicant respectfully requests that this application be taken out of order pursuant to 37 C.F. R. §1.496(b).

In the Specification:

Please add the following paragraph after the title on page 1:

-- This application is the United States National Stage of International Application No. PCT/US00/26870 filed September 29, 1999, and is also a continuation of United States Application No. 09/408,584, filed September 29, 1999, now issued as United States Patent No. \_\_\_\_\_, each hereby incorporated by reference. --

In the claims:

Please cancel without prejudice claims: 1-41 and 201-202.

Claims 42-200 each satisfying the criteria of PCT Articles 33(1)-(4) as to novelty, inventive step and industrial applicability are set out below as a clean version of the claims as amended for the convenience of the examiner beginning on the next separate page:

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42. A kit for intranasal delivery, comprising:
  - a. a dose;
  - b. a diluent in which said dose may be combined; and
  - c. an intranasal device comprising:
    - i. an intranasal probe having a dose delivery aperture;
    - ii. a dose administrator having a first end and a second end, wherein said first end is responsive to said intranasal probe; and
    - iii. an intranasal probe coupler responsive to said intranasal probe and said first end of said dose administrator, wherein said intranasal probe coupler has at least one aperture which communicates between said dose administrator and said intranasal probe.
43. An intranasal delivery device as described in claim 42, further comprising a force application element coupled to said second end of said flexible dose administrator.
44. An intranasal delivery device as described in claim 42, wherein said dose comprises a material selected from the group consisting of: an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26EC to about 30EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39EC, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39EC, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No.2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.

45. An equine intranasal delivery device as described in claim 43, wherein said force application element is a syringe.
46. An intranasal delivery device as described in claim 45, wherein said dose administrator comprises a flexible material.
47. An intranasal delivery device as described in claim 42, further comprising a dose-location coordinate indicator responsive to said flexible dose administrator.
48. An equine intranasal delivery device as described in claim 47, wherein said dose-location coordinate indicator has a position which assures a dose-location coordinate temperature between about 26<sup>N</sup> C to about 34<sup>N</sup> C.
49. An intranasal delivery device as described in claim 42, further comprising a force dissemination contact surface having hebetated termini responsive to said exterior surface of said intranasal probe.
50. An intranasal delivery device as described in claim 42, further comprising a conformable dose sequestration element having a dose sequestration volume sufficient to sequester said dose.
51. An intranasal delivery device as described in claim 50, wherein said conformable dose sequestration element further comprises a dose retainer, wherein said dose retainer positions said dose proximate to said dose delivery aperture.
52. An intranasal delivery device as described in claim 42, further comprising a stream delivery element coupled to said dose delivery aperture.



53. An equine intranasal delivery device, comprising:
- a dose administrator;
  - a force application element coupled to said dose administrator; and
  - a an equine influenza cold-adapted live virus derived from strain A/equine/Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No.2627) dose responsive to said force application element.
54. An equine intranasal delivery device as described in claim 53, further comprising a dose diluent, wherein said dose and said dose diluent are combined.
55. An equine intranasal delivery device as described in claim 54, wherein said force application element is a syringe.
56. An equine intranasal delivery device as described in claim 55, further comprising a coupler element having a first end responsive to said dose administrator and a second end responsive to said force application element, wherein said coupler element has at least one aperture which communicates between a volume of said dose administrator and said force application element.
57. An equine intranasal delivery device as described in claim 56, further comprising an intranasal probe coupled to said dose administrator.
58. An equine intranasal delivery device as described in claim 57, further comprising an intranasal probe coupler having a first end responsive to said intranasal probe and a second end responsive to said dose administrator, wherein said intranasal probe coupler has at least one aperture which communicates between said volume of said dose administrator and an exterior surface of said intranasal probe.

59. An equine intranasal delivery device as described in claim 58, wherein said dose administrator comprises a flexible material.
60. An intranasal delivery device, comprising:
- a dose administrator;
  - a force application element coupled to said dose administrator; and
  - a dose responsive to said force application element.
61. An intranasal delivery device as described in claim 60, further comprising a dose diluent, wherein said dose and said dose diluent are combined.
62. An intranasal delivery device as described in claim 61, wherein said force application element is a syringe.
63. An intranasal delivery device as described in claim 62, further comprising a coupler element having a first end responsive to said dose administrator and a second end responsive to said force application element, wherein said coupler element has at least one aperture which communicates between a volume of said dose administrator and said force application element.
64. An intranasal delivery device as described in claim 63, further comprising an intranasal probe coupled to said dose administrator.
65. An intranasal delivery device as described in claim 64, further comprising an intranasal probe coupler having a first end responsive to said intranasal probe and a second end responsive to said dose administrator, wherein said intranasal probe coupler has at least one aperture which communicates between said volume of said dose administrator and an exterior surface of said intranasal probe.

66. An intranasal delivery device as described in claim 65, wherein said dose administrator comprises a flexible material.
67. An intranasal delivery device as described in claim 60, wherein said dose comprises a material selected from the group consisting of: an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26EC to about 30EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39EC, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39EC, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No. 2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.
68. A method for producing an equine intranasal delivery device, comprising the steps of:
- providing a dose delivery aperture element;
  - coupling an intranasal probe to said dose delivery aperture;
  - joining a flexible dose administrator having a first end and a second end to said intranasal probe by said first end; and
  - coupling a conformable dose sequestration element having a dose sequestration volume which communicates with said dose delivery aperture element.
69. A method for producing an equine intranasal delivery device as described in claim 68, further comprising the step of coupling a force application element to said fluid dose propellant.

70. A method for producing an equine intranasal delivery device as described in claim 69, further comprising the step of separating said conformable dose sequestration element having a dose sequestration volume from said force application element with a fluid dose propellant.
71. A method for producing an equine intranasal delivery device as described in claim 60, further comprising the step of coupling a force dissemination contact surface having hebetated termini to said intranasal probe.
72. A method for producing an equine intranasal delivery device as described in claim 61, further comprising the step of providing a stream delivery element.
73. A method for producing an equine intranasal delivery device as described in claim 62, further comprising the step of positioning a dose-location coordinate indicator at a location on said flexible dose administrator, wherein said location of said dose-location coordinate indicator assures delivery of said dose to a target which is susceptible to said dose.
74. A method for producing an equine intranasal delivery device as described in claim 73, further comprising the step of joining an axial collapse protection element coupled to said flexible dose administrator.
75. A method for producing an equine intranasal delivery device as described in claim 74, further comprising coupling an intranasal probe coupler to said intranasal probe and to said flexible dose administrator, wherein said intranasal probe coupler has at least one aperture which communicates between said volume of said conformable dose sequestration element and said dose delivery aperture.
76. A method for producing an equine intranasal delivery device as described in claim 75, further comprising the step of coupling a fluid dose propellant coupler to said conformable

dose sequestration element and to said dose propellant, wherein said fluid dose propellant coupler has at least one aperture which communicates between said volume of said conformable dose sequestration element and said fluid dose propellant.

77. A method for producing an equine intranasal delivery device as described in claim 76, further comprising the step of selecting a dose from the group consisting of: a substance, a composition, a therapeutic composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen which elicits an immune response, a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26EC to about 30EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39EC, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39EC, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR2625), EIV-P824 (identified by accession No. ATCC VR2624), MSV+5 (identified by accession No. 2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.
78. A method for producing an equine intranasal delivery device as described in claim 77, further comprising the step of sequestering a dose within said dose sequestration volume of said conformable dose sequestration element.
79. A method for producing an equine intranasal delivery device as described in claim 78, wherein said step of sequestering said dose within said volume of said conformable dose

sequestration element further comprises:

- a. establishing a volume of diluent containing said dose within said volume of said conformable dose sequestration element;
- b. removing said volume of diluent from said dose; and
- c. leaving a dry dose within said dose sequestration volume of said conformable dose sequestration element.

80. A method for producing an equine intranasal delivery device as described in claim 78, wherein said step of sequestering said dose within said interior volume of said flexible dose sequestration element further comprises:

- a. establishing a volume of diluent containing said dose within said volume of said conformable dose sequestration element;
- b. establishing conditions within said volume of diluent containing said dose wherein said dose does not substantially degrade.

81. A method of equine intranasal delivery, comprising the steps of:

- a. sequestering a dose within a conformable dose sequestration element, wherein said conformable dose sequestration element separates said dose from a force application element with a volume of a fluid dose propellant;
- b. positioning an intranasal probe within a nostril of an equid;
- c. sliding said intranasal probe up said nostril of said equid;
- d. terminating sliding of said intranasal probe up said nostril;
- e. propelling said dose from said conformable dose sequestration element; and
- f. delivering said dose onto a target of said equid.

82. A method of intranasal delivery as described in claim 81, wherein said step of delivering said dose onto said target of said equid comprises streaming said dose onto said target of said

equid.

83. A method of intranasal delivery as described in claim 82, wherein said step of sequestering a dose within a conformable dose sequestration element, further comprises the steps of:
  - a. establishing at least one dose in a volume of diluent;
  - b. submerging said dose delivery aperture into said volume of diluent containing at least one dose; and
  - c. reducing pressure within said conformable dose sequestration element sufficient to transfer said dose established in said volume of diluent into said conformable dose sequestration element.
84. A method of intranasal delivery as described in claim 83, further comprising the step of retaining said dose within said conformable dose sequestration element adjacent to said intranasal probe.
85. A method of intranasal delivery as described in claim 84, further comprising the step of guiding said intranasal probe so as to not enter an opening to a false nostril.
86. A method of intranasal delivery as described in claim 81, further comprising the step of positioning a dose-location coordinate indicator into proximity with an exterior portion of said nostril of said equid.
87. A method of intranasal delivery as described in claim 86, wherein said step of positioning a dose-location coordinate indicator into proximity with an exterior portion of said nostril of said equid assures a dose-location coordinate having a temperature of about 26EC to about 34EC
88. A method of intranasal delivery as described in any one of claims 87, wherein said step of propelling said dose from said conformable dose sequestration element further comprises the

steps of:

- a. measuring a fluid dose propellant volume, wherein said volume of said fluid dose propellant is in excess of a volume of a minimum dose delivery volume;
- b. propelling said dose from said volume of said conformable dose sequestration element with a portion of said dose propellant volume; and
- c. chasing said dose with a remaining portion of said dose propellant volume.

89. An equine intranasal delivery device as described in claim 88, wherein said dose comprises a substance selected from the group consisting of: a substance, a composition, a therapeutic composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen which elicits an immune response, a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26EC to about 30EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39EC, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39EC, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/Kentucky/1/91 (H3N8), EIV-P821 (identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No. 2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.

90. An intranasal delivery device, comprising:
- a. a force application element;
  - b. a conformable dose sequestration element having a dose sequestration volume sufficiently large to sequester a dose, wherein said conformable dose sequestration



element separates said dose from said force application element; and

- c. a fluid dose propellant which separates said conformable dose sequestration element from said force application element.

- 91. An intranasal delivery device as described in claim 90, further comprising an intranasal probe responsive to said conformable dose sequestration element.
- 92. An intranasal delivery device as described in claim 91, further comprising a dose delivery aperture element coupled to said intranasal probe.
- 93. An intranasal delivery device as described in claim 92, further comprising a stream delivery element coupled to said dose delivery aperture element.
- 94. An intranasal delivery device as described in claim 93, wherein said stream delivery element has a diameter of about 0.75 millimeters (about 0.030 inches).
- 95. An intranasal delivery device as described in claim 94, further comprising a flexible dose administrator having a cylindrical exterior surface.
- 96. An intranasal delivery device as described in claim 95, wherein said cylindrical exterior surface of said flexible dose administrator has a radius of 3 millimeters (about 0.125 inches).
- 97. An intranasal delivery device as described in claim 96, wherein said cylindrical exterior surface of said flexible administrator has a length of about 150 millimeters (about 5.9 inches).
- 98. An intranasal delivery device as described in claim 97, further comprising a force dissemination contact surface having hebetated termini responsive to said intranasal probe.

99. An intranasal delivery device as described in claim 98, wherein said force dissemination contact surface responsive to said intranasal probe comprises a sphere cap wherein said sphere cap and a cylindrical exterior surface of said flexible dose administrator form a contiguous surface.
100. An intranasal delivery device as described in claim 99, wherein said sphere cap has a radius of about 3 millimeters (about 0.125 inches) and a sphere cap height of about 1 millimeters (about 0.040 inches) and wherein said cylindrical exterior surface has a radius of about 3 millimeters (about 0.125 inches).
101. An intranasal delivery device as described in claim 100, wherein said intranasal probe and said force dissemination contact surface have a unitized construction.
102. An intranasal delivery device as described in claim 101, wherein said conformable dose sequestration element further comprises a dose retainer, wherein said dose retainer positions said dose contained within said volume of solvent proximate to said dose delivery aperture.
103. An intranasal delivery device as described in claim 102, wherein said dose retainer is a capillary.
104. An intranasal delivery device as described in claim 103, wherein said capillary has a diameter of about 3 millimeters (about 0.125 inches).
105. An intranasal delivery device as described in claim 104, wherein said volume of diluent is about 1 milliliter.
106. An intranasal delivery device as described in claim 105, wherein said fluid dose propellant has a volume in a range of about 1 milliliters to about 3 milliliters.

107. An intranasal delivery device as described in claim 106, further comprising a dose-location coordinate indicator coupled to said dose sequestration element.
108. An intranasal delivery device as described in claim 107, wherein said dose-location coordinate indicator comprises a visually enhanced surface coupled to said exterior surface of said dose sequestration element.
109. An intranasal delivery device as described in claim 108, wherein said visually enhanced surface coupled to said exterior surface of said dose sequestration element comprises an annular projection.
110. An equine intranasal delivery device as described in claim 109, wherein said dose-location coordinate indicator has a position which assures a dose-location coordinate temperature between about 26<sup>N</sup> C to about 34<sup>N</sup> C.
111. An intranasal delivery device as described in claim 110, wherein said dose-location coordinate indicator has a position at about 150 millimeters (about 5.9 inches) from said first end of said dose sequestration element.
112. An intranasal delivery device as described in claim 111, further comprising an axial collapse prevention element coupled to said dose sequestration element.
113. An intranasal delivery device as described in claim 112, wherein said axial collapse prevention element comprises a flexibly resilient layer between said exterior cylindrical surface of said flexible dose administrator and said volume of said conformable dose sequestration element.
114. An intranasal delivery device as described in claim 113, further comprising an intranasal probe coupler having a first end responsive to said intranasal probe and a second end

responsive to said dose sequestration element, wherein said intranasal probe coupler has at least one aperture which communicates between said volume of said conformable dose sequestration element and said dose delivery aperture.

115. An intranasal delivery device as described in claim 114, wherein said second end of said intranasal probe coupler comprises an annular barb engaged to said interior surface of said conformable dose sequestration element.
116. An intranasal delivery device as described in claim 115, wherein said intranasal probe coupler and intranasal probe comprise unitized construction.
117. An intranasal delivery device as described in claim 116, wherein said intranasal probe coupler, said intranasal probe, and said force dissemination contact surface having hebetated termini comprise unitized construction.
118. An intranasal delivery device as described in claim 117, further comprising a propellant coupler having a first end responsive to said interior volume of said dose sequestration element and a second end responsive to said fluid dose propellant, wherein said propellant coupler has at least one aperture which communicates between said interior volume of said conformable dose sequestration element and said fluid dose propellant.
119. An intranasal delivery device as described in claim 118, wherein said first end of said propellant coupler comprises an annular barb engaged to said interior surface of said conformable dose sequestration element.
120. An intranasal delivery device as described in claim 119, wherein said second end of said propellant coupler comprises a syringe adaptor.
121. An intranasal delivery device as described in claim 120, wherein said syringe adaptor

comprises a luer-lock.

122. An intranasal delivery device as described in claim 121, wherein said propellant coupler, and said dose-location coordinate indicator comprise unitized construction.
123. An intranasal delivery device as described in claim 122, wherein said force application element is a syringe.
124. An equine intranasal delivery device as described in claim 123, wherein said dose comprises a substance selected from the group consisting of: a composition, a therapeutic composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen which elicits an immune response, a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26EC to about 30EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39EC, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39EC, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821 (identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No. 2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.
125. An intranasal delivery device as described in claim 124, further comprising an equid.
126. A method of delivering a dose intranasally, comprising the steps of:

- a. sequestering a dose within an dose sequestration element, wherein said dose sequestration element separates said dose from a force application element with a volume of a fluid dose propellant;
- b. measuring a volume of fluid dose propellant, wherein said volume is in excess of a minimum delivery volume of said dose;
- c. applying force to said volume of said fluid dose propellant;
- d. propelling said dose from said interior volume of said dose sequestration element;
- e. delivering said dose to a target susceptible to said dose; and
- f. expelling a remaining portion of said volume of said fluid dose propellant from said conformable dose sequestration element.

127. A method of intranasal delivery as described in claim 126, wherein said step of delivering said dose to said target susceptible to said dose comprises streaming said dose onto said target susceptible to said dose.

128. A method of intranasal delivery as described in claim 127, wherein said step of sequestering said dose within said interior volume of said dose sequestration element further comprises:

- a. establishing at least one dose in a volume of diluent;
- b. submerging said dose sequestration element into said volume of solvent containing said at least one dose; and
- c. reducing pressure within said volume of said conformable dose sequestration element sufficiently to transfer said dose into said interior volume of said conformable dose sequestration element.

129. A method of intranasal delivery as described in claim 128, wherein establishing said at least one dose within said volume of said conformable dose sequestration element further comprises retaining said dose in a position by capillary forces.

130. A method of intranasal delivery as described in claim 129, further comprising the step of

providing an intranasal probe responsive to said conformable dose sequestration element.

131. A method of intranasal delivery as described in claim 130, further comprising the step of providing a flexible dose administrator responsive to said conformable dose sequestration element.
132. A method of intranasal delivery as described in claim 131, further comprising the step of sliding said intranasal probe up a nostril of an animal.
133. A method of intranasal delivery as described in claim 132, further comprising the step of guiding said intranasal probe so as to not enter an opening to a false nostril.
134. A method of intranasal delivery as described in claim 133, further comprising the step of positioning a dose-location coordinate indicator into proximity with an exterior portion of said nostril of said animal.
135. A method of intranasal delivery as described in claim 134, wherein said step of positioning a dose-location coordinate indicator into proximity with an exterior portion of said nostril of said equid assures a dose-location coordinate having a temperature of about 26EC to about 34EC
136. A method of intranasal delivery as described in claim 135, further comprising the step of terminating sliding of said intranasal probe up said nostril of said animal.
137. A method of intranasal delivery as described in claim 136, further comprising the step of administering said dose to said target of an equid.
138. An equine intranasal delivery device as described in claim 137, further comprising the step of selecting said from the group consisting of: a composition, a therapeutic composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen

which elicits an immune response, a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26EC to about 30EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39EC, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39EC, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821 (identified by accession No. ATCC VR2625), EIV-P824 (identified by accession No. ATCC VR2526), MSV+5 (identified by accession No.2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.

139. An intranasal dose delivery device, comprising:
  - a. a stream delivery element;
  - b. a dose delivery aperture element coupled to said stream delivery element;
  - c. an intranasal probe responsive to said dose delivery aperture;
  - d. a flexible dose administrator;
  - e. an intranasal probe coupler having a first end responsive to said intranasal probe and a second end responsive to said flexible dose administrator, wherein said intranasal probe coupler has at least one aperture which communicates between said intranasal probe and said stream delivery element;
  - f. a force application element responsive to said flexible dose administrator; and
  - g. a force application element coupler having a first end responsive to said flexible dose administrator and a second end responsive to said force application element, wherein said force application coupler has at least one aperture which communicates between said flexible dose administration element and said force application element.



140. An intranasal delivery device as described in claim 139, wherein said stream delivery element has an aperture having a diameter of about 0.75 millimeters (about 0.030 inches).
141. An intranasal delivery device as described in claim 140, wherein said flexible dose administrator has a cylindrical exterior surface.
142. An intranasal delivery device as described in claim 141, wherein said cylindrical exterior surface has a diameter of about 6 millimeters (about 0.250 inches).
143. An intranasal delivery device as described in claim 142, wherein said cylindrical exterior surface has a length of about 150 millimeters (about 5.9 inches).
144. An intranasal delivery device as described in claim 143, further comprising a force dissemination contact surface having a tapered terminus coupled to said intranasal probe.
145. An intranasal delivery device as described in claim 144, wherein said force dissemination contact surface responsive to said flexible intranasal probe comprises a sphere cap, wherein said sphere cap and said cylindrical exterior surface of said flexible dose administrator form a contiguous surface.
146. An intranasal delivery device as described in claim 145, wherein said sphere cap has a radius of about 3 millimeters (about 0.125 inches) and a sphere cap height of about 1 millimeters (about 0.040 inches).
147. An intranasal delivery device as described in claim 146, wherein said intranasal probe and said force dissemination contact surface have a unitized construction.
148. An intranasal delivery device as described in claim 139, further comprising a conformable

dose sequestration element having a dose sequestration volume responsive to said flexible dose administrator.

149. An intranasal delivery device as described in claim 148, wherein said conformable dose sequestration element further comprises a dose retainer, wherein said dose retainer has a location proximate to said stream delivery element.
150. An intranasal delivery device as described in claim 149, wherein said dose retainer comprises a capillary.
151. An intranasal delivery device as described in claim 150, wherein said capillary has a diameter of 3 millimeters (about 0.125 inches).
152. An intranasal delivery device as described in claim 151, further comprising an axial collapse prevention element coupled to said flexible dose administrator.
153. An intranasal delivery device as described in claim 152, wherein said axial collapse prevention element comprises a resiliently flexible layer between said cylindrical exterior surface of said flexible dose administrator and said conformable dose sequestration element.
154. An intranasal delivery device as described in claim 153, wherein said resiliently flexible layer comprises polyvinyl chloride having a thickness of about 1.5 millimeters (0.040 inches).
155. An intranasal delivery device as described in claim 154, further comprising a dose-location coordinate indicator coupled to said flexible dose administrator.
156. An intranasal delivery device as described in claim 155, wherein said dose-location coordinate indicator comprises a visually enhanced surface.

157. An intranasal delivery device as described in claim 156, wherein said visually enhanced surface comprises an annular projection.
158. An equine intranasal delivery device as described in claim 157, wherein said dose-location coordinate indicator has a position which assures a dose-location coordinate temperature between about 26<sup>N</sup> C to about 34<sup>N</sup> C.
159. An intranasal delivery device as described in claim 158, wherein said dose-location coordinate indicator has a position on said flexible intranasal probe distal from said stream delivery element of about 150 millimeters (about 5.9 inches).
160. An intranasal delivery device as described in claim 159, further comprising a fluid dose propellant which separates said conformable dose sequestration element from said force application element.
161. An intranasal delivery device as described in claim 160, wherein said flexible dose administrator and said dose sequestration element have a unitized construction.
162. An intranasal delivery device as described in claim 161, wherein said second end of said intranasal probe coupler comprises an annular barb engaged to said interior surface of said flexible dose administrator.
163. An intranasal delivery device as described in claim 162, wherein said intranasal probe coupler and intranasal probe comprise unitized construction.
164. An intranasal delivery device as described in claim 163, wherein said intranasal probe coupler, said intranasal probe, and said force dissemination contact surface having hebetated termini comprise unitized construction.

165. An intranasal delivery device as described in claim 164, wherein said first end of said propellant coupler comprises an annular barb engaged to said interior surface of said flexible dose administrator.
166. An intranasal delivery device as described in claim 165, wherein said second end of said force application element coupler comprises a syringe adaptor.
167. An intranasal delivery device as described in claim 166, wherein said syringe adaptor comprises a luer-lock.
168. An intranasal delivery device as described in claim 167, wherein said force application element coupler and said dose-location coordinate indicator comprise unitized construction.
169. An intranasal delivery device as described in claim 168, further comprising a dose responsive to said stream delivery element.
170. An equine intranasal delivery device as described in claim 169, wherein said dose comprises a substance selected from the group consisting of: a composition, a therapeutic composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen which elicits an immune response, a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26EC to about 30EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39EC, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39EC, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91

(H3N8), EIV-P821 (identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No. 2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.

171. An intranasal delivery device as described in claim 170, further comprising a volume of diluent, wherein said volume of diluent and said dose are combined.
172. An intranasal delivery device as described in claim 171, further comprising an equid.
173. A method of delivering a dose intranasally, comprising the steps of:
  - a. establishing a dose in a volume of diluent within a flexible administrator;
  - b. positioning said flexible administrator within a nostril of an animal;
  - c. applying force to said dose in said volume of diluent;
  - d. propelling said dose in said volume of diluent from a stream delivery element; and
  - e. streaming said dose in said volume of diluent onto a target susceptible to said dose.
174. A method of delivering a dose intranasally as described in claim 173, wherein steps d and e occur simultaneously.
175. A method of delivering a dose intranasally as described in claim 174, further comprising the step of providing a flexible dose administrator responsive to said intranasal probe.
176. A method of delivering a dose intranasally as described in claim 175, further comprising the step of sliding said flexible dose administrator up a nostril of an animal.
177. A method of delivering a dose intranasally as described in claim 176, further comprising the step of disseminating the force of contact between said flexible dose administrator and a

nasal passage of said animal.

178. A method of delivering a dose intranasally as described in claim 177, further comprising the step of preventing axial collapse of said flexible dose administrator.
179. A method of delivering a dose intranasally as described in claim 178, further comprising the step of positioning a dose-location coordinate indicator into proximity with an exterior portion of said nostril of said animal.
180. A method of intranasal delivery as described in claim 179, wherein said step of positioning a dose-location coordinate indicator into proximity with an exterior portion of said nostril of said equid assures a dose-location coordinate having a temperature of about 26EC to about 34EC
181. A method of delivering a dose intranasally as described in claim 180, further comprising the step of terminating sliding of said flexible dose administrator up said nostril of said animal.
182. A method of delivering a dose intranasally as described in claim 181, further comprising the step of sequestering a dose in a volume of a conformable dose sequestration element, wherein said conformable dose sequestration element separates said dose from a force application element with a volume of fluid dose propellant.
183. A method of delivering a dose intranasally as described in claim 182, further comprising the step of measuring a volume of fluid dose propellant, wherein said volume of fluid dose propellant has a volume in excess of a minimum dose delivery volume.
184. A method of delivering a dose intranasally as described in claim 183, further comprising chasing said dose with said volume in excess of said minimum dose delivery volume.

185. A method of intranasal delivery as described in claim 184, wherein said step of sequestering said dose within said interior volume of said dose sequestration element further comprises:
- establishing at least one dose in a volume of diluent;
  - submerging said conformable dose sequestration element into said volume of diluent containing said at least one dose; and
  - reducing pressure within said volume of said conformable dose sequestration element sufficiently to transfer said dose into said dose sequestration volume of said conformable dose sequestration element.
186. A method of intranasal delivery as described in claim 185, wherein establishing said at least one dose within said volume of said conformable dose sequestration element further comprises retaining said dose in a position proximate to said stream delivery element by capillary forces.
187. A method of intranasal delivery as described in claim 186, further comprising the step of administering said dose to an equid.
188. A method of intranasal delivery as described in claim 187, further comprising the step of guiding said flexible dose administrator so as to not enter an opening to a false nostril.
189. An equine intranasal delivery device as described in claim 188, wherein said dose comprises a substance selected from the group consisting of: a composition, a therapeutic composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen which elicits an immune response, a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26EC to about 30EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39EC, a equine cold-

adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39EC, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821 (identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No. 2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.

190. An intranasal delivery device, comprising:
- a. a dose administrator having a volume;
  - b. an intranasal probe coupled to said dose administrator;
  - c. an intranasal probe coupler having a first end responsive to said intranasal probe and a second end responsive to said dose administrator, wherein said intranasal probe coupler has at least one aperture which communicates between said volume of said dose administrator and an exterior surface of said intranasal probe;
  - d. a force application element coupled to said dose administrator;
  - e. a coupler element having a first end responsive to said dose administrator and a second end responsive to said force application element, wherein said coupler element has at least one aperture which communicates between [a] said volume of said dose administrator and said force application element;
  - f. a dose-location coordinate indicator responsive to said [flexible] dose administrator; and
  - g. a dose.
191. An intranasal delivery device as described in claim 190, further comprising a force dissemination contact surface having hebetated termini responsive to said exterior surface of said intranasal probe.



192. An intranasal delivery device as described in claim 191, further comprising a fluid dose propellant which separates said dose from said force application element.
193. An intranasal delivery device as described in claim 192, further comprising a conformable dose sequestration element having a sequestration volume sufficient to sequester said dose, wherein said sequestration volume communicates with said dose delivery aperture element and said fluid dose propellant.
194. An intranasal delivery device as described in claim 193, wherein said fluid dose propellant has a greater volume than a minimum dose delivery volume.
195. An intranasal delivery device as described in claim 194, wherein said conformable dose sequestration element further comprises a dose retainer, wherein said dose retainer positions said dose proximate to said dose delivery aperture.
196. An intranasal delivery device as described in claim 195, further comprising a stream delivery element coupled to said dose delivery aperture.
197. An intranasal delivery device as described in claim 196, wherein said dose comprises a substance selected from the group consisting of: a composition, a therapeutic composition, a prophylactic composition, a drug, an immunogen, an immunogen which elicits an immune response, a protein, a nucleic acid, a live virus, or a reassortant live virus.
198. An equine intranasal delivery device as described in claim 197, wherein said dose-location coordinate indicator has a position which assures a dose-location coordinate temperature between about 26<sup>N</sup> C to about 34<sup>N</sup> C.
199. An intranasal delivery device as described in claim 198, wherein said dose comprises a substance selected from the group consisting of: a live virus, a reassortant live virus, a cold-

adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26EC to about 30EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39EC, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39EC, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5(identified by accession No. 2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.

200. An intranasal delivery device as described in claim 199, further comprising a dose diluent, wherein said dose and said dose diluent are combined.

## REMARKS

The above-identified patent application is the United States national stage of international PCT Patent Application No. PCT/US00/26870. The United States was designated as the International Search Authority and as the International Preliminary Examining Authority. The original PCT application included claims 1-202 each satisfying the criteria of PCT Article 33(1)-(4) as to novelty, inventive step and industrial applicability. The applicant has amended claims 67, 69, 70, 76, 81, 88, 118, 119, 120, 122, 126, 160, 165, 182, 183, and 190 in the application only to the extent necessary to eliminate objections as to form. The applicant has without prejudice cancelled claims 1-41 which were the subject matter of United States Application No. 09/408,584. The applicant has further canceled claims 201 and 202 to eliminate any objection as to form. The applicant respectfully requests examination of remaining claims 42-200.

When all the claims in an PCT application satisfy each of the criteria of PCT Article 33(1)-(4) and when the applicant only amends the claims to the extent necessary to eliminate objections as to form or to cancel rejected claims the applicant may pay the fee set forth in 37 C.F.R. §1.492(a)(4) and request that the application be taken out of order pursuant to 37 C.F. R. §1.496(b). As such, the applicant has paid the fee as set forth in 37 C.F.R. §1.492(a)(4) and the applicant respectfully requests that this application be taken out of order for examination.

The application was considered to have met the requirement of unity of invention throughout the international search and the international examination and no invitation to pay additional fees was made under Article 17 (3)(a). During the national stage of a PCT application when considering unity of invention of claims under 35 U.S.C. §§121, 371, and 372; Rule 13.1 and 13.2 will be followed without regard to the practice in national applications filed under 35 U.S.C. 111 and §1850 MPEP. Unity of invention is present when there is a "technical relationship" among the claimed inventions involving one or more of the same or corresponding "special technical features". Rule 13.2 PCT. The expression "special technical features" means those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. Rule 13.2 PCT. Moreover, the rules specifically allow for inventions within the same application

when there is a relationship between a product, process, and use §1850 C (A). Illustrations of Particular Situations.

In the original application, an unusually large number of claims were presented in order to adequately claim the various aspects of the present invention(s) in dependent and alternatively independent fashions. The applicant has voluntarily reduced the number of claims by cancellation of claims 1-41 and 201-202 as filed in the original application, leaving only claims 42-200 for examination, including several closely related independent claims having unity of invention along with their dependent claims.

Thus, the applicants have voluntarily reduced the number of claims to assist the examiners in their efforts and to expedite the examination. The voluntary reduction in claim number is not to be construed as a waiver of any right to file other applications such as continuations, divisions, continuations-in-part, or similar applications and have the remaining claims examined without any reduction in breadth. The applicant respectfully requests that each of claims 42-200 be examined as single group as part of this United States National Stage application.

The applicant has set out a clean version of the claims above and a version with markings to show changes made pursuant to 37 C.F.R. §1.121 beginning on the next separate. The applicant respectfully requests allowance of the claims at the examiner's earliest convenience.

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Claims 1-41 Cancelled without prejudice.

42. A kit for intranasal delivery, comprising:
- a. a dose;
  - b. a diluent in which said dose may be combined; and
  - c. an intranasal device comprising:
    - i. an intranasal probe having a dose delivery aperture;
    - ii. a dose administrator having a first end and a second end, wherein said first end is responsive to said intranasal probe; and
    - iii. an intranasal probe coupler responsive to said intranasal probe and said first end of said dose administrator, wherein said intranasal probe coupler has at least one aperture which communicates between said dose administrator and said intranasal probe.
43. An intranasal delivery device as described in claim 42, further comprising a force application element coupled to said second end of said flexible dose administrator.
44. An intranasal delivery device as described in claim 42, wherein said dose comprises a material selected from the group consisting of: an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26EC to about 30EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39EC, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39EC, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by

accession No.2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.

45. An equine intranasal delivery device as described in claim 43, wherein said force application element is a syringe.
46. An intranasal delivery device as described in claim 45, wherein said dose administrator comprises a flexible material.
47. An intranasal delivery device as described in claim 42, further comprising a dose-location coordinate indicator responsive to said flexible dose administrator.
48. An equine intranasal delivery device as described in claim 47, wherein said dose-location coordinate indicator has a position which assures a dose-location coordinate temperature between about 26<sup>N</sup>C to about 34<sup>N</sup> C.
49. An intranasal delivery device as described in claim 42, further comprising a force dissemination contact surface having hebetated termini responsive to said exterior surface of said intranasal probe.
50. An intranasal delivery device as described in claim 42, further comprising a conformable dose sequestration element having a dose sequestration volume sufficient to sequester said dose.
51. An intranasal delivery device as described in claim 50, wherein said conformable dose sequestration element further comprises a dose retainer, wherein said dose retainer positions said dose proximate to said dose delivery aperture.
52. An intranasal delivery device as described in claim 42, further comprising a stream

delivery element coupled to said dose delivery aperture.

53. An equine intranasal delivery device, comprising:
- a. a dose administrator;
  - b. a force application element coupled to said dose administrator; and
  - c. an equine influenza cold-adapted live virus derived from strain A/equine/Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No.2627) dose responsive to said force application element.
54. An equine intranasal delivery device as described in claim 53, further comprising a dose diluent, wherein said dose and said dose diluent are combined.
55. An equine intranasal delivery device as described in claim 54, wherein said force application element is a syringe.
56. An equine intranasal delivery device as described in claim 55, further comprising a coupler element having a first end responsive to said dose administrator and a second end responsive to said force application element, wherein said coupler element has at least one aperture which communicates between a volume of said dose administrator and said force application element.
57. An equine intranasal delivery device as described in claim 56, further comprising an intranasal probe coupled to said dose administrator.
58. An equine intranasal delivery device as described in claim 57, further comprising an intranasal probe coupler having a first end responsive to said intranasal probe and a second end responsive to said dose administrator, wherein said intranasal probe coupler has at least one aperture which communicates between said volume of said dose administrator and an exterior surface of said intranasal probe.

59. An equine intranasal delivery device as described in claim 58, wherein said dose administrator comprises a flexible material.
60. An intranasal delivery device, comprising:
- a. a dose administrator;
  - b. a force application element coupled to said dose administrator; and
  - c. a dose responsive to said force application element.
61. An intranasal delivery device as described in claim 60, further comprising a dose diluent, wherein said dose and said dose diluent are combined.
62. An intranasal delivery device as described in claim 61, wherein said force application element is a syringe.
63. An intranasal delivery device as described in claim 62, further comprising a coupler element having a first end responsive to said dose administrator and a second end responsive to said force application element, wherein said coupler element has at least one aperture which communicates between a volume of said dose administrator and said force application element.
64. An intranasal delivery device as described in claim 63, further comprising an intranasal probe coupled to said dose administrator.
65. An intranasal delivery device as described in claim 64, further comprising an intranasal probe coupler having a first end responsive to said intranasal probe and a second end responsive to said dose administrator, wherein said intranasal probe coupler has at least one aperture which communicates between said volume of said dose administrator and an exterior surface of said intranasal probe.
66. An intranasal delivery device as described in claim 65, wherein said dose



administrator comprises a flexible material.

67. An intranasal delivery device as described in [any one of] claim[s] 60, wherein said dose comprises a material selected from the group consisting of: an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26EC to about 30EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39EC, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39EC, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No. 2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.
68. A method for producing an equine intranasal delivery device, comprising the steps of:
- providing a dose delivery aperture element;
  - coupling an intranasal probe to said dose delivery aperture;
  - joining a flexible dose administrator having a first end and a second end to said intranasal probe by said first end; and
  - coupling a conformable dose sequestration element having a dose sequestration volume which communicates with said dose delivery aperture element.
69. A method for producing an equine intranasal delivery device as described in claim 68, further comprising the step of coupling a force application element to said fluid

dose [propellent] propellant.

70. A method for producing an equine intranasal delivery device as described in claim 69, further comprising the step of separating said conformable dose sequestration element having a dose sequestration volume from said force application element with a fluid dose [propellent] propellant.
71. A method for producing an equine intranasal delivery device as described in claim 60, further comprising the step of coupling a force dissemination contact surface having hebetated termini to said intranasal probe.
72. A method for producing an equine intranasal delivery device as described in claim 61, further comprising the step of providing a stream delivery element.
73. A method for producing an equine intranasal delivery device as described in claim 62, further comprising the step of positioning a dose-location coordinate indicator at a location on said flexible dose administrator, wherein said location of said dose-location coordinate indicator assures delivery of said dose to a target which is susceptible to said dose.
74. A method for producing an equine intranasal delivery device as described in claim 73, further comprising the step of joining an axial collapse protection element coupled to said flexible dose administrator.
75. A method for producing an equine intranasal delivery device as described in claim 74, further comprising coupling an intranasal probe coupler to said intranasal probe and to said flexible dose administrator, wherein said intranasal probe coupler has at least one aperture which communicates between said volume of said conformable dose sequestration element and said dose delivery aperture.
76. A method for producing an equine intranasal delivery device as described in claim

75, further comprising the step of coupling a fluid dose [propellent] propellant coupler to said conformable dose sequestration element and to said dose [propellent] propellant, wherein said fluid dose [propellent] propellant coupler has at least one aperture which communicates between said volume of said conformable dose sequestration element and said fluid dose [propellent] propellant.

77. A method for producing an equine intranasal delivery device as described in claim 76, further comprising the step of selecting a dose from the group consisting of: a substance, a composition, a therapeutic composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen which elicits an immune response, a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26EC to about 30EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39EC, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39EC, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR2625), EIV-P824 (identified by accession No. ATCC VR2624), MSV+5 (identified by accession No. 2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.
78. A method for producing an equine intranasal delivery device as described in claim 77, further comprising the step of sequestering a dose within said dose sequestration volume of said conformable dose sequestration element.

79. A method for producing an equine intranasal delivery device as described in claim 78, wherein said step of sequestering said dose within said volume of said conformable dose sequestration element further comprises:
  - a. establishing a volume of diluent containing said dose within said volume of said conformable dose sequestration element;
  - b. removing said volume of diluent from said dose; and
  - c. leaving a dry dose within said dose sequestration volume of said conformable dose sequestration element.
80. A method for producing an equine intranasal delivery device as described in claim 78, wherein said step of sequestering said dose within said interior volume of said flexible dose sequestration element further comprises:
  - a. establishing a volume of diluent containing said dose within said volume of said conformable dose sequestration element;
  - b. establishing conditions within said volume of diluent containing said dose wherein said dose does not substantially degrade.
81. A method of equine intranasal delivery, comprising the steps of:
  - a. sequestering a dose within a conformable dose sequestration element, wherein said conformable dose sequestration element separates said dose from a force application element with a volume of a fluid dose [propellant] propellant;
  - b. positioning an intranasal probe within a nostril of an equid;
  - c. sliding said intranasal probe up said nostril of said equid;
  - d. terminating sliding of said intranasal probe up said nostril;
  - e. propelling said dose from said conformable dose sequestration element; and
  - f. delivering said dose onto a target of said equid.
82. A method of intranasal delivery as described in claim 81, wherein said step of delivering said dose onto said target of said equid comprises streaming said dose onto said target of said equid.

83. A method of intranasal delivery as described in claim 82, wherein said step of sequestering a dose within a conformable dose sequestration element, further comprises the steps of:
- establishing at least one dose in a volume of diluent;
  - submerging said dose delivery aperture into said volume of diluent containing at least one dose; and
  - reducing pressure within said conformable dose sequestration element sufficient to transfer said dose established in said volume of diluent into said conformable dose sequestration element.
84. A method of intranasal delivery as described in claim 83, further comprising the step of retaining said dose within said conformable dose sequestration element adjacent to said intranasal probe.
85. A method of intranasal delivery as described in claim 84, further comprising the step of guiding said intranasal probe so as to not enter an opening to a false nostril.
86. A method of intranasal delivery as described in claim 81, further comprising the step of positioning a dose-location coordinate indicator into proximity with an exterior portion of said nostril of said equid.
87. A method of intranasal delivery as described in claim 86, wherein said step of positioning a dose-location coordinate indicator into proximity with an exterior portion of said nostril of said equid assures a dose-location coordinate having a temperature of about 26EC to about 34EC
88. A method of intranasal delivery as described in any one of claims 87, wherein said step of propelling said dose from said conformable dose sequestration element further comprises the steps of:
- measuring a fluid dose [propellant] propellant volume, wherein said volume

of said fluid dose [propellent] propellant is in excess of a volume of a minimum dose delivery volume;

- b. propelling said dose from said volume of said conformable dose sequestration element with a portion of said dose [propellent] propellant volume; and
- c. chasing said dose with a remaining portion of said dose [propellent] propellant volume.

89. An equine intranasal delivery device as described in claim 88, wherein said dose comprises a substance selected from the group consisting of: a substance, a composition, a therapeutic composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen which elicits an immune response, a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26EC to about 30EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39EC, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39EC, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No.2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.

90. An intranasal delivery device, comprising:
- a. a force application element;

- b. a conformable dose sequestration element having a dose sequestration volume sufficiently large to sequester a dose, wherein said conformable dose sequestration element separates said dose from said force application element; and
- c. a fluid dose [propellent] propellant which separates said conformable dose sequestration element from said force application element.

- 91. An intranasal delivery device as described in claim 90, further comprising an intranasal probe responsive to said conformable dose sequestration element.
- 92. An intranasal delivery device as described in claim 91, further comprising a dose delivery aperture element coupled to said intranasal probe.
- 93. An intranasal delivery device as described in claim 92, further comprising a stream delivery element coupled to said dose delivery aperture element.
- 94. An intranasal delivery device as described in claim 93, wherein said stream delivery element has a diameter of about 0.75 millimeters (about 0.030 inches).
- 95. An intranasal delivery device as described in claim 94, further comprising a flexible dose administrator having a cylindrical exterior surface.
- 96. An intranasal delivery device as described in claim 95, wherein said cylindrical exterior surface of said flexible dose administrator has a radius of 3 millimeters (about 0.125 inches).
- 97. An intranasal delivery device as described in claim 96, wherein said cylindrical exterior surface of said flexible administrator has a length of about 150 millimeters (about 5.9 inches).
- 98. An intranasal delivery device as described in claim 97, further comprising a force

dissemination contact surface having hebetated termini responsive to said intranasal probe.

99. An intranasal delivery device as described in claim 98, wherein said force dissemination contact surface responsive to said intranasal probe comprises a sphere cap wherein said sphere cap and a cylindrical exterior surface of said flexible dose administrator form a contiguous surface.
100. An intranasal delivery device as described in claim 99, wherein said sphere cap has a radius of about 3 millimeters (about 0.125 inches) and a sphere cap height of about 1 millimeters (about 0.040 inches) and wherein said cylindrical exterior surface has a radius of about 3 millimeters (about 0.125 inches).
101. An intranasal delivery device as described in claim 100, wherein said intranasal probe and said force dissemination contact surface have a unitized construction.
102. An intranasal delivery device as described in claim 101, wherein said conformable dose sequestration element further comprises a dose retainer, wherein said dose retainer positions said dose contained within said volume of solvent proximate to said dose delivery aperture.
103. An intranasal delivery device as described in claim 102, wherein said dose retainer is a capillary.
104. An intranasal delivery device as described in claim 103, wherein said capillary has a diameter of about 3 millimeters (about 0.125 inches).
105. An intranasal delivery device as described in claim 104, wherein said volume of diluent is about 1 milliliter.
106. An intranasal delivery device as described in claim 105, wherein said fluid dose



[propellent] propellant has a volume in a range of about 1 milliliters to about 3 milliliters.

107. An intranasal delivery device as described in claim 106, further comprising a dose-location coordinate indicator coupled to said dose sequestration element.
108. An intranasal delivery device as described in claim 107, wherein said dose-location coordinate indicator comprises a visually enhanced surface coupled to said exterior surface of said dose sequestration element.
109. An intranasal delivery device as described in claim 108, wherein said visually enhanced surface coupled to said exterior surface of said dose sequestration element comprises an annular projection.
110. An equine intranasal delivery device as described in claim 109, wherein said dose-location coordinate indicator has a position which assures a dose-location coordinate temperature between about 26<sup>N</sup> C to about 34<sup>N</sup> C.
111. An intranasal delivery device as described in claim 110, wherein said dose-location coordinate indicator has a position at about 150 millimeters (about 5.9 inches) from said first end of said dose sequestration element.
112. An intranasal delivery device as described in claim 111, further comprising an axial collapse prevention element coupled to said dose sequestration element.
113. An intranasal delivery device as described in claim 112, wherein said axial collapse prevention element comprises a flexibly resilient layer between said exterior cylindrical surface of said flexible dose administrator and said volume of said conformable dose sequestration element.
114. An intranasal delivery device as described in claim 113, further comprising an

intranasal probe coupler having a first end responsive to said intranasal probe and a second end responsive to said dose sequestration element, wherein said intranasal probe coupler has at least one aperture which communicates between said volume of said conformable dose sequestration element and said dose delivery aperture.

115. An intranasal delivery device as described in claim 114, wherein said second end of said intranasal probe coupler comprises an annular barb engaged to said interior surface of said conformable dose sequestration element.
116. An intranasal delivery device as described in claim 115, wherein said intranasal probe coupler and intranasal probe comprise unitized construction.
117. An intranasal delivery device as described in claim 116, wherein said intranasal probe coupler, said intranasal probe, and said force dissemination contact surface having hebetated termini comprise unitized construction.
118. An intranasal delivery device as described in claim 117, further comprising a [propellent] propellant coupler having a first end responsive to said interior volume of said dose sequestration element and a second end responsive to said fluid dose propellent, wherein said [propellent] propellant coupler has at least one aperture which communicates between said interior volume of said conformable dose sequestration element and said fluid dose [propellent] propellant.
119. An intranasal delivery device as described in claim 118, wherein said first end of said [propellent] propellant coupler comprises an annular barb engaged to said interior surface of said conformable dose sequestration element.
120. An intranasal delivery device as described in claim 119, wherein said second end of said [propellent] propellant coupler comprises a syringe adaptor.
121. An intranasal delivery device as described in claim 120, wherein said syringe

adaptor comprises a luer-lock.

122. An intranasal delivery device as described in claim 121, wherein said [propellent] propellant coupler, and said dose-location coordinate indicator comprise unitized construction.
123. An intranasal delivery device as described in claim 122, wherein said force application element is a syringe.
124. An equine intranasal delivery device as described in claim 123, wherein said dose comprises a substance selected from the group consisting of: a composition, a therapeutic composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen which elicits an immune response, a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26EC to about 30EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39EC, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39EC, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No. 2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.
125. An intranasal delivery device as described in claim 124, further comprising an equid.

126. A method of delivering a dose intranasally, comprising the steps of:
- sequestering a dose within an dose sequestration element, wherein said [conformable] dose sequestration element separates said dose from a force application element with a volume of a fluid dose [propellent] propellant;
  - measuring a volume of fluid dose [propellent] propellant, wherein said volume is in excess of a minimum delivery volume of said dose;
  - applying force to said volume of said fluid dose [propellent] propellant;
  - propelling said dose from said interior volume of said dose sequestration element;
  - delivering said dose to a target susceptible to said dose; and
  - expelling a remaining portion of said volume of said fluid dose [propellent] propellant from said conformable dose sequestration element.
127. A method of intranasal delivery as described in claim 126, wherein said step of delivering said dose to said target susceptible to said dose comprises streaming said dose onto said target susceptible to said dose.
128. A method of intranasal delivery as described in claim 127, wherein said step of sequestering said dose within said interior volume of said dose sequestration element further comprises:
- establishing at least one dose in a volume of diluent;
  - submerging said dose sequestration element into said volume of solvent containing said at least one dose; and
  - reducing pressure within said volume of said conformable dose sequestration element sufficiently to transfer said dose into said interior volume of said conformable dose sequestration element.
129. A method of intranasal delivery as described in claim 128, wherein establishing said at least one dose within said volume of said conformable dose sequestration element further comprises retaining said dose in a position by capillary forces.

130. A method of intranasal delivery as described in claim 129, further comprising the step of providing an intranasal probe responsive to said conformable dose sequestration element.
131. A method of intranasal delivery as described in claim 130, further comprising the step of providing a flexible dose administrator responsive to said conformable dose sequestration element.
132. A method of intranasal delivery as described in claim 131, further comprising the step of sliding said intranasal probe up a nostril of an animal.
133. A method of intranasal delivery as described in claim 132, further comprising the step of guiding said intranasal probe so as to not enter an opening to a false nostril.
134. A method of intranasal delivery as described in claim 133, further comprising the step of positioning a dose-location coordinate indicator into proximity with an exterior portion of said nostril of said animal.
135. A method of intranasal delivery as described in claim 134, wherein said step of positioning a dose-location coordinate indicator into proximity with an exterior portion of said nostril of said equid assures a dose-location coordinate having a temperature of about 26EC to about 34EC
136. A method of intranasal delivery as described in claim 135, further comprising the step of terminating sliding of said intranasal probe up said nostril of said animal.
137. A method of intranasal delivery as described in claim 136, further comprising the step of administering said dose to said target of an equid.
138. An equine intranasal delivery device as described in claim 137, further comprising the step of selecting said from the group consisting of: a composition, a therapeutic

composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen which elicits an immune response, a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26EC to about 30EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39EC, an equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39EC, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821 (identified by accession No. ATCC VR2625), EIV-P824 (identified by accession No. ATCC VR2526), MSV+5 (identified by accession No.2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.

139. An intranasal dose delivery device, comprising:
  - a. a stream delivery element;
  - b. a dose delivery aperture element coupled to said stream delivery element;
  - c. an intranasal probe responsive to said dose delivery aperture;
  - d. a flexible dose administrator;
  - e. an intranasal probe coupler having a first end responsive to said intranasal probe and a second end responsive to said flexible dose administrator, wherein said intranasal probe coupler has at least one aperture which communicates between said intranasal probe and said stream delivery element;
  - f. a force application element responsive to said flexible dose administrator; and
  - g. a force application element coupler having a first end responsive to said

flexible dose administrator and a second end responsive to said force application element, wherein said force application coupler has at least one aperture which communicates between said flexible dose administration element and said force application element.

140. An intranasal delivery device as described in claim 139, wherein said stream delivery element has an aperture having a diameter of about 0.75 millimeters (about 0.030 inches).
141. An intranasal delivery device as described in claim 140, wherein said flexible dose administrator has a cylindrical exterior surface.
142. An intranasal delivery device as described in claim 141, wherein said cylindrical exterior surface has a diameter of about 6 millimeters (about 0.250 inches).
143. An intranasal delivery device as described in claim 142, wherein said cylindrical exterior surface has a length of about 150 millimeters (about 5.9 inches).
144. An intranasal delivery device as described in claim 143, further comprising a force dissemination contact surface having hebetated termini coupled to said intranasal probe.
145. An intranasal delivery device as described in claim 144, wherein said force dissemination contact surface responsive to said flexible intranasal probe comprises a sphere cap, wherein said sphere cap and said cylindrical exterior surface of said flexible dose administrator form a contiguous surface.
146. An intranasal delivery device as described in claim 145, wherein said sphere cap has a radius of about 3 millimeters (about 0.125 inches) and a sphere cap height of about 1 millimeters (about 0.040 inches).
147. An intranasal delivery device as described in claim 146, wherein said intranasal

probe and said force dissemination contact surface have a unitized construction.

148. An intranasal delivery device as described in [any one of] claim[s] 139 [or 146], further comprising a conformable dose sequestration element having a dose sequestration volume responsive to said flexible dose administrator.
149. An intranasal delivery device as described in claim 148, wherein said conformable dose sequestration element further comprises a dose retainer, wherein said dose retainer has a location proximate to said stream delivery element.
150. An intranasal delivery device as described in claim 149, wherein said dose retainer comprises a capillary.
151. An intranasal delivery device as described in claim 150, wherein said capillary has a diameter of 3 millimeters (about 0.125 inches).
152. An intranasal delivery device as described in claim 151, further comprising an axial collapse prevention element coupled to said flexible dose administrator.
153. An intranasal delivery device as described in claim 152, wherein said axial collapse prevention element comprises a resiliently flexible layer between said cylindrical exterior surface of said flexible dose administrator and said conformable dose sequestration element.
154. An intranasal delivery device as described in claim 153, wherein said resiliently flexible layer comprises polyvinyl chloride having a thickness of about 1.5 millimeters (0.040 inches).
155. An intranasal delivery device as described in claim 154, further comprising a dose-location coordinate indicator coupled to said flexible dose administrator.



156. An intranasal delivery device as described in claim 155, wherein said dose-location coordinate indicator comprises a visually enhanced surface.
157. An intranasal delivery device as described in claim 156, wherein said visually enhanced surface comprises an annular projection.
158. An equine intranasal delivery device as described in claim 157, wherein said dose-location coordinate indicator has a position which assures a dose-location coordinate temperature between about 26<sup>N</sup> C to about 34<sup>N</sup> C.
159. An intranasal delivery device as described in claim 158, wherein said dose-location coordinate indicator has a position on said flexible intranasal probe distal from said stream delivery element of about 150 millimeters (about 5.9 inches).
160. An intranasal delivery device as described in claim 159, further comprising a fluid dose [propellent] propellant which separates said conformable dose sequestration element from said force application element.
161. An intranasal delivery device as described in claim 160, wherein said flexible dose administrator and said dose sequestration element have a unitized construction.
162. An intranasal delivery device as described in claim 161, wherein said second end of said intranasal probe coupler comprises an annular barb engaged to said interior surface of said flexible dose administrator.
163. An intranasal delivery device as described in claim 162, wherein said intranasal probe coupler and intranasal probe comprise unitized construction.
164. An intranasal delivery device as described in claim 163, wherein said intranasal probe coupler, said intranasal probe, and said force dissemination contact surface having hebetated termini comprise unitized construction.

165. An intranasal delivery device as described in claim 164, wherein said first end of said [propellent] propellant coupler comprises an annular barb engaged to said interior surface of said flexible dose administrator.
166. An intranasal delivery device as described in claim 165, wherein said second end of said force application element coupler comprises a syringe adaptor.
167. An intranasal delivery device as described in claim 166, wherein said syringe adaptor comprises a leur-lock.
168. An intranasal delivery device as described in claim 167, wherein said force application element coupler and said dose-location coordinate indicator comprise unitized construction.
169. An intranasal delivery device as described in claim 168, further comprising a dose responsive to said stream delivery element.
170. An equine intranasal delivery device as described in claim 169, wherein said dose comprises a substance selected from the group consisting of: a composition, a therapeutic composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen which elicits an immune response, a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26EC to about 30EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37EC, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39EC, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39EC, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from

strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No.2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.

171. An intranasal delivery device as described in claim 170, further comprising a volume of diluent, wherein said volume of diluent and said dose are combined.
172. An intranasal delivery device as described in claim 171, further comprising an equid.
173. A method of delivering a dose intranasally, comprising the steps of:
  - a. establishing a dose in a volume of diluent within a flexible administrator;
  - b. positioning said flexible administrator within a nostril of an animal;
  - c. applying force to said dose in said volume of diluent;
  - d. propelling said dose in said volume of diluent from a stream delivery element; and
  - e. streaming said dose in said volume of diluent onto a target susceptible to said dose.
174. A method of delivering a dose intranasally as described in claim 173, wherein steps d and e occur simultaneously.
175. A method of delivering a dose intranasally as described in claim 174, further comprising the step of providing a flexible dose administrator responsive to said intranasal probe.
176. A method of delivering a dose intranasally as described in claim 175, further comprising the step of sliding said flexible dose administrator up a nostril of an animal.

177. A method of delivering a dose intranasally as described in claim 176, further comprising the step of disseminating the force of contact between said flexible dose administrator and a nasal passage of said animal.
178. A method of delivering a dose intranasally as described in claim 177, further comprising the step of preventing axial collapse of said flexible dose administrator.
179. A method of delivering a dose intranasally as described in claim 178, further comprising the step of positioning a dose-location coordinate indicator into proximity with an exterior portion of said nostril of said animal.
180. A method of intranasal delivery as described in claim 179, wherein said step of positioning a dose-location coordinate indicator into proximity with an exterior portion of said nostril of said equid assures a dose-location coordinate having a temperature of about 26EC to about 34EC
181. A method of delivering a dose intranasally as described in claim 180, further comprising the step of terminating sliding of said flexible dose administrator up said nostril of said animal.
182. A method of delivering a dose intranasally as described in claim 181, further comprising the step of sequestering a dose in a volume of a conformable dose sequestration element, wherein said conformable dose sequestration element separates said dose from a force application element with a volume of fluid dose [propellent] propellant.
183. A method of delivering a dose intranasally as described in claim 182, further comprising the step of measuring a volume of fluid dose [propellent] propellant, wherein said volume of fluid dose [propellent] propellant has a volume in excess of a minimum dose delivery volume.

184. A method of delivering a dose intranasally as described in claim 183, further comprising chasing said dose with said volume in excess of said minimum dose delivery volume.
185. A method of intranasal delivery as described in claim 184, wherein said step of sequestering said dose within said interior volume of said dose sequestration element further comprises:
- a. establishing at least one dose in a volume of diluent;
  - b. submerging said conformable dose sequestration element into said volume of diluent containing said at least one dose; and
  - c. reducing pressure within said volume of said conformable dose sequestration element sufficiently to transfer said dose into said dose sequestration volume of said conformable dose sequestration element.
186. A method of intranasal delivery as described in claim 185, wherein establishing said at least one dose within said volume of said conformable dose sequestration element further comprises retaining said dose in a position proximate to said stream delivery element by capillary forces.
187. A method of intranasal delivery as described in claim 186, further comprising the step of administering said dose to an equid.
188. A method of intranasal delivery as described in claim 187, further comprising the step of guiding said flexible dose administrator so as to not enter an opening to a false nostril.
189. An equine intranasal delivery device as described in claim 188, wherein said dose comprises a substance selected from the group consisting of: a composition, a therapeutic composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen which elicits an immune response, a live virus,



administrator; and  
g.[.] a dose[;].

191. An intranasal delivery device as described in claim 190, further comprising a force dissemination contact surface having hebetated termini responsive to said exterior surface of said intranasal probe.
192. An intranasal delivery device as described in claim 191, further comprising a fluid dose [propellent] propellant which separates said dose from said force application element.
193. An intranasal delivery device as described in claim 192, further comprising a conformable dose sequestration element having a sequestration volume sufficient to sequester said dose, wherein said sequestration volume communicates with said dose delivery aperture element and said fluid dose [propellent] propellant.
194. An intranasal delivery device as described in claim 193, wherein said fluid dose propellent has a greater volume than a minimum dose delivery volume.
195. An intranasal delivery device as described in claim 194, wherein said conformable dose sequestration element further comprises a dose retainer, wherein said dose retainer positions said dose proximate to said dose delivery aperture.
196. An intranasal delivery device as described in claim 195, further comprising a stream delivery element coupled to said dose delivery aperture.
197. An intranasal delivery device as described in claim 196, wherein said dose comprises a substance selected from the group consisting of: a composition, a therapeutic composition, a prophylactic composition, a drug, an immunogen, an immunogen which elicits an immune response, a protein, a nucleic acid, a live virus, or a reassortant live virus.

198. An equine intranasal delivery device as described in claim 197, wherein said dose-location coordinate indicator has a position which assures a dose-location coordinate temperature between about 26°C to about 34°C.
199. An intranasal delivery device as described in claim 198, wherein said dose comprises a substance selected from the group consisting of: a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26°C to about 30°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39°C, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39°C, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821 (identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No. 2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.
200. An intranasal delivery device as described in claim 199, further comprising a dose diluent, wherein said dose and said dose diluent are combined.

Claims 201 and 202 canceled without prejudice.



## CONCLUSION

Claims 1-41 and 201-202 have been cancelled without prejudice. Claims 42-200 remain in the application. Each of claims 42-200 satisfy the criteria of PCT Article 33(1)-(4), have unity of invention, and have only been amended to the extent necessary to eliminate objections as to form or to cancel rejected claims. The applicant having satisfied the requirements of 37 C.F. R. §1.496(b), and unity of invention, respectfully requests that the application be taken out of order and that claims 42-200 be examined as a single group.

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Respectfully Submitted,

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# INTRANASAL DELIVERY SYSTEM

## I. TECHNICAL FIELD

This invention relates to an equine intranasal delivery system for the delivery of cold-adapted equine viruses. The invention also includes both apparatus and methods for the intranasal delivery of various materials, compositions or medicaments to both humans and animals. Generally, the invention provides basic technology for the delivery of various compositions to target locations.

## II. BACKGROUND

There are many advantages to intranasal administration of medications and other compositions which include, among others, a direct route to the blood stream, avoidance of hepatic first pass metabolism, bioavailability, ease and convenience, and proximity to the central nervous system. See Y.W. Chien et al., *Anatomy and Physiology of the Nose*, Nasal Systemic Drug Delivery, Chapter 1, 1-26, 1989. Various types of compositions, therapeutics, prophylactics or otherwise, may be delivered intranasally including, but not limited to, topical anesthetics, sedatives, hypnotics, analgesics, ketamines, opiates, glucagons, vaccines, anti-nausea and motion sickness medications, antihistamines, antihypertensive drugs, psychoactive medications, antibiotics, and hormones. See, as examples, M.R. Nott et al., *Topical Anaesthesia for the Insertion of Nasogastric Tubes*, European Journal of Anaesthesiology, 12(3), May 1995; R.J. Henry et al, *A pharmacokinetic Study of Midazolam in Dogs: Nasal Drop Versus Atomizer Administration*, Journal of the American Academy of Pediatric Dentistry, 20(5), 321-326, 1998; J. Lithander et al., *Sedation with nasal Ketamine and Midazolam for Cryotherapy in Retinopathy of Prematurity*, British Journal of Ophthalmology, 77(8), 529-530, 1993; F.E. Ralley, *Intranasal Opiates: Old Route For New Drugs*, Canadian Journal of Anesthesiology, 36(5) 491-493, 1989; B. Haneberg et al, *Intranasal Administration of Mengiocoecal outer membrane vesicle vaccine induces persistent local Mucosal Antibodies and Serum Antibodies with Strong Bactericidal Activity in Humans*, Infection and Immunity, 66(4), 1334-1341, 1998; B.K. Wager et al, *A Double Blind Placebo-Controlled Evaluation of Intranasal Metoclopramide in the Prevention of Postoperative nausea and Vomiting*, Pharmacotherapy, 16(6), 1063-1069 1996; and J.Q. Wang, et al., *An Experimental Study on*

*Nasal Absorption of Gentamycin in Dogs*, Chinese Medical Journal, 107(3), 219-221, 1994.

- Specifically with respect to live virus vaccines, it has been shown that they are often too pathogenic for use as immunogens for either humans or animals as described in United States Patent No. 3,953,592. Attempts to vaccinate against viral infection with inactivated
- 5 virus, however, may not offer effective protection and can produce undesirable side effects as indicated in United States Patent 3,953,592; R. Belshe et al, *Immunization of Infants and Young Children with Live Attenuated Trivalent Cold-Recombinant Influenza A H1N1, H3N2, and B Vaccine*, The Journal of Infectious Disease, Volume 165, 727-732, 1992; K.M. Nelson et al., *Local and Systemic Isotype-specific Antibody Responses to Equine Influenza*
- 10 *Virus Infection Versus Conventional Vaccination*, Vaccine, Volume 16, Number 13, 1998. Injection of equids with inactivated viruses may cause, for example, inflammatory reactions at the site of injection. See Mumford et al., *Serological Methods for Identification of Slowly-Growing Herpesviruses Isolated from the Respiratory Tract of Horses*, Equine Infectious Disease IV, 49-52, 1978; Mumford et al., *Consultation on Newly Emerging*
- 15 *Strains of Equine Influenza*, Vaccine 11, 1172-1174, 1993. It has also been shown that protective responses to viral infection are not limited to the production of antibodies but that a local antibody system and an interferon production mechanism operate at the primary site of infection in the nasal passage membranes as disclosed by United States Patent No. 4,132,775; T. Tomoda et al., *Prevention of Influenza by the Intranasal Administration of*
- 20 *Cold-Recombinant, Live-attenuated Influenza Virus Vaccine: Importance of Interferon- $\gamma$  Production and Local IgA Response*, Vaccine, Volume 13, Number 2, 185-190, 1995; and Holmes, Lamb, Coggins, et al, *Live Temperature Sensitive Equine-2 Influenza A Virus Vaccine: Production and Efficacy in Experimental Ponies*, Equine infectious disease VI, 253-258, 1992.
- 25 As such, intranasal delivery of the above mentioned compositions has become a preferred route of administration for both inactivated viruses as described by United States Patent 3,953,592, and cold-adapted live virus vaccines which are inhibited from replication in the range of the normal body temperature but do replicate at lower temperatures, such as perhaps, associated with the mucosae of the upper respiratory tract as disclosed by United
- 30 States Patent No. 3,927, 208; Maassab, et al., *Biologic and Immunologic Characteristics of Cold-Adapted Influenza Virus*, Journal of Immunology. 102, 728-732, 1969; and Keitel et al., *Trivalent Attenuated Cold-Adapted Virus Vaccine: Reduced Viral Shedding and Serum*

Antibody Responses in Susceptible Adults, The Journal of Infectious Disease, Volume 167, 305-311, 1993. Intranasal delivery of compositions has also been effective for certain reassortant cold-adapted viruses which may also possess a dominant interference phenotype which may inhibit the growth of the corresponding wild-type strains and other heterologous viruses as disclosed by United States Patent Nos. 4,683,137 and 4,693,893.

Due to the increased use of intranasal delivery of various compositions, including inactivated and cold-adapted live viruses, in both humans and animals, there is corresponding demand in the marketplace for intranasal apparatus and methods of intranasal delivery which address existing problems, and which are especially acute with respect to equids including, for example, horses, ponies, or exotic equids such as zebra which may be part of a zoological collection, or otherwise.

A significant problem with intranasal delivery of compositions is interspecies and intraspecies anatomical variation. With regard to one aspect of these differences, it is evident from casual observation that the gross morphology of bovine species present a shorter nasal passage than, for example, equid species. An inflexible intranasal administrator, for example, may be adequate for intranasal delivery of a composition or dose to a bovine where the intranasal administrator need only tranverse a short distance in the bovine nasal passage, however, such an inflexible device may not be suitable for equids where the intranasal administrator may have to traverse several inches within the nasal passages of an equid.

A related problem with intranasal delivery of compositions in equids as opposed to bovine, for example, is the presence of a false nostril (nasal diverticulum) as described by Klaus, Dieter, Budras, *Anatomy of the Horse an Illustrated Text*, 2nd edition, Mosby-Wolfe, London, 1994. The nasal diverticulum presents two problems with regard to intranasal delivery in equids although other species may have anatomical structures which present equivalent difficulties. First, an intranasal probe for equids must be designed such that the user has an immediate means of determining if the delivery aperture of the intranasal probe has properly entered the nasal passage or if the intranasal probe has inadvertently entered the nasal diverticulum. The second problem associated with the nasal diverticulum is that the type of cells which line the nasal diverticulum are not the same type of cells which line the nasal passage of the upper respiratory tract. Delivery of compositions, including the delivery of cold-adapted live viruses, to the type of cells which line the nasal diverticulum

may not provide therapy because such cells may not be susceptible to such compositions, or cold adapted live viruses. While the nasal diverticulum provides a remarkable example of the necessity of coordinating therapeutic compositions with an anatomical location having cells susceptible to a particular composition or dose, dose-location coordination may be an  
5 important aspect of intranasal delivery in many other species.

Another significant problem with intranasal delivery is the movement and regional distribution of the composition or dose subsequent to administration. The deposition of a composition or dose after intranasal delivery depends upon particle inertia, sedimentation due to gravity, and diffusion due to Brownian motion. M. Dolovich, *Principles Underlying*  
10 *Aerosol Therapy*, Journal of Aerosol Medicine, Vol. 2, No. 2, 1989; see also A. Brown and J. Slusser, *Propellant-driven Aerosols of Function Proteins as Potential Therapeutic Agents in the Respiratory Tract*, Immunopharmacology 28, 241-257, 1994. Each of these mechanisms can be dependent upon the particle size of the dose or composition delivered. As disclosed by M. Dolovich, particles having a diameter of less than about 1 micrometer  
15 can remain suspended as the time required for the particle to diffuse to an airway wall tends to be greater than the time to complete the inspiratory phase of a normal breath. Optimum deposition in the lung may be achieved with particles having a diameter of about 3 micrometers. Larger particles having a diameter of greater than about 5 micrometers are often deposited in the upper airways. M. Dolovich, at pages 173-174. As such the proper  
20 particle size should be selected depending on where in the airway or lung compartment deposition is to occur. With respect to cold-adapted viruses delivered intranasally from devices designed to provide a fine aerosol or heterodisperse aerosol, a portion of the dose may remain suspended in the respired air and subsequently exhaled without deposition. This may be particularly true when treating animals which may not be instructed to hold their  
25 breath. Alternately, the cold-adapted virus having a somewhat larger particle size may remain suspended and then deposited in the lung compartment. Once in the lung compartment the virus may be prohibited from replication by exposure to the normal body temperature of the animal. In either event, a portion of the dose may be rendered ineffective because the dose was delivered as a particle of non-optimal size.

30 To the extent that "multiple studies show that atomized pump is the best nasal delivery system because it gives a constant dose and a very good mucosal distribution" and that research has demonstrated "clearance of spray is much slower than clearance of drops",

these studies, research and marketing descriptions, teach away from a non-aerosol-location coordinated intranasal delivery system. See T. Wolfe, *Intranasal Medication Administration: Literature Review*, Wolf Tory Medical, Incorporated, <http://www.wolfetory.com/intr.html>, 1-17, at page 3, 1999.

5 A related problem is coordinating the delivery of a particular type of composition with a particular location of delivery. Often the location to which the dose is to be administered is hidden from view. As such, there may be little assurance that the composition has actually been delivered to the proper location or target. This may be particularly problematic for those individuals that have little or no formal medical training.

10 Yet another problem with existing devices for intranasal administration of compounds is generation of excess physical stimulation of the nasal passage as the intranasal probe or dose administrator is guided along the intranasal passage. This physical stimulation may be more acute when the force used to move the intranasal probe along the intranasal passage is translated to a tip of the dose administrator having a small surface area which  
15 contacts the nasal mucosae. As can be understood, an intranasal administrator comprising a relatively small diameter tube with a thin sidewall may be more likely to irritate, cut, score or pierce the intranasal surface causing the human or animal to move unpredictably. After the intranasal passage has been injured it may also subsequently become infected and require additional medical attention. Moreover, when attempting to administer a composition or  
20 dose intranasally to a human or an animal, unpredicted movement caused by such physical stimulation may force the intranasal dose administrator into contact with the eye or perhaps into contact with the person attempting to administer the composition or dose. This inadvertant movement may also transfer biological fluids between the patient and the practitioner or cause the loss of a portion or all of the composition or dose. As such,  
25 reducing physical stimulation of the spot contacted by the intranasal probe may be preferred.

Another problem related to intranasal administrators which have a small diameter or thin wall construction is that axial deflection of the intranasal administrator may be excessive under the typical forces encountered during use. Axial collapse of the administrator may may result in a failure to deliver the dose properly, additional physical  
30 stimulation of the intranasal passage, or cause injury.

Still another significant problem is the amount of composition or dose that may remain in devices upon delivery of the composition or dose to the patient. This "dead

volume" within the device represents an amount of the dose or composition that is unavailable to the patient. With regard to some types of jet nebulizers, this may amount to as much as 0.5-1.0 milliliters of concentrated solution, as disclosed by M. Dolovich, *Physical Principles Underlying Aerosol Therapy*, Journal of Aerosol Medicine, Volume 2, Number 2, 1989. The dead volume associated with intranasal devices having administrators or intranasal probes designed for equids, for example, which are quite long may have a similarly large dead volume. Even if devices with a smaller dead volume were designed, even such smaller volume of a composition or a dose made unavailable to the patient may be significant where the cost of the dose is high. An intranasal delivery system which reduces dead volume by design of the intranasal device or by the method of use may provide substantial benefit.

Another problem with some delivery systems may be a lack of unitized construction. Components which may have been produced as a single unit may comprise several component parts which are compression fit together, or bonded together with use of a solvent, as can be understood from the Misty device. These several component parts may disassemble during intranasal administration or subsequently become lodged in the intranasal passage of the human or animal. These component parts may cause immediate injury or remain in the intranasal passages undiscovered to cause subsequent injury. Removal of these component parts from the intranasal passages may also require additional medical procedures.

From the consumer's point of view there are several problems which have not been adequately addressed by existing systems for the administration of compositions. The first is the fear of needles. Many people are needle phobic and as a result many people are not inoculated. S. Hoffert, *Biotech Innovations Aim to Conquer Influenza Virus*, The Scientist, 1 and 6, March 2, 1998. A second problem for the consumer is the potential for inadvertent needle sticks which may transfer either the composition or physiological fluids from the patient to the person administering the composition or dose. A third problem for the consumer is proper disposal of needles. A delivery device which eliminates injection of the composition with a needle may induce the needle phobic to obtain inoculation and may also address the problems of inadvertent needle sticks and needle disposal. A fourth problem for the consumer untrained in medical or veterinary fields is the fear of self administration of compositions to themselves, or other humans or animals. A part of this fear may be the

use of needles, or other devices, which the consumer believes may cause injury to the patient due to the consumer's lack of training. However, even with respect to delivery devices which may be designed for use without a needle, the consumer may have concerns that the composition or dose may be delivered in a manner that is not therapeutic for the patient. A  
5 properly engineered intranasal device may address these consumer concerns by providing features which assure proper measurement of a dose and delivery of the dose to an intranasal location in a manner which will be therapeutically effective.

As to each of these problems regarding devices for the delivery of compositions and the methods of delivering compositions, the present invention discloses technology which  
10 overcomes every one of the problems disclosed in a practical fashion.

### III. DISCLOSURE OF THE INVENTION

Accordingly, the broad goal of the invention is to provide a delivery system for various compositions including medicaments which safely and effectively delivers the entire  
15 amount of a composition or a dose to the proper target. Specifically, the broad goal of the invention also addresses the particular requirements of intranasal delivery of such compositions and medicaments in the equine field which is particularly difficult due to the size, mobility and disposition of equids. The composition or dose delivery features disclosed are varied and may be incorporated into a variety of devices or used in numerous  
20 applications. Naturally, as a result of these several different and potentially independent aspects of the invention, the objects of the invention are quite varied.

One of the broad objects of the invention is to provide basic technology to improve the delivery of a wide variety of compositions, including medicaments, across a broad range of commercial, research, medical and veterinary applications.

25 Another object of the invention, is to provide specific apparatus and methods for the intranasal delivery of prophylactic and therapeutic compositions to both humans and animals incorporating the above mentioned basic technological aspects of the invention.

Another object of the invention is to define the scope of existing technology that may be improved by using such technology with specific strains of cold-adapted equine influenza  
30 virus.

Another object of the invention is to provide an intranasal delivery device for equids which specifically incorporates certain aspects of the invention so as to accommodate the



longer or more complicated nasal passages of the equine anatomy.

Related to this object are certain embodiments of the invention which provide for the effective delivery of compositions or doses, including particular cold-adapted influenza or cold-adapted equine influenza viruses, to specific dose-location coordinates which may be  
5 hidden from visual observation. A particular goal is to provide apparatus and methods for assuring that specific strains of equine cold-adapted equine influenza viruses may be delivered to a location on the nasal mucosa of an equid having a temperature range suitable for replication of these specific equine influenza strains.

Another object of the invention is to provide an element which prevents the axial  
10 collapse of the dose administrator due to incidental contact as it is brought into position for delivery of the composition or dose to the target.

Another object of the invention is to provide delivery of the composition or dose in a manner which assures that a substantial portion of such composition or dose will remain in the proximity of the desired dose-location coordinate or target.

15 Another object of the invention is to minimize the cutting, scoring or other injuries and physical stimulation from the incidental contact of various surfaces, including intranasal passages, with the dose administrator as it is positioned for delivery of the composition or dose.

Another object of the invention is to minimize the amount of the dose which is  
20 retained by the dose delivery administrator after delivery of the composition or dose to the dose-location coordinate or target. Specifically, with respect to devices which have larger dead volumes or larger minimum dose delivery volumes, such as those which have longer dose administrators, this aspect of the invention allows the dose to be sequestered proximate to the dose delivery aperture. A sequestered dose come into contact with less surface area  
25 of the delivery system and is expelled from the dose administrator with a lower minimum delivery volume.

Another object of the invention is to make an uncomplicated delivery device which may be used by individuals that have little or no formal training. A goal related to this object is elimination of parts which may inadvertently become disassembled during the use  
30 of the device. Naturally further objects of the invention are disclosed throughout other areas of the specification and claims.

#### IV. BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a drawing showing an elevation of a particular embodiment of the invention.

Figure 2 is a drawing showing a top view of a particular embodiment of the invention.

Figure 3 is a drawing showing a bottom view of a particular embodiment of the invention.

Figure 4 is a drawing showing a cross section of a particular embodiment of an intranasal probe and dose administrator.

Figure 5 is a drawing showing a cross section of a particular embodiment of a dose administrator having a conformable dose sequestration element.

Figure 6 is a drawing showing an elevation of a particular embodiment of a unitized construct having an intranasal probe, a force dissemination contact surface, a dose delivery aperture element, a stream delivery element, and an intranasal probe coupler.

Figure 7 shows an elevation of a particular embodiment of the delivery system.

Figure 8 is a drawing showing a cross section of a particular embodiment of the fluid dose propellant coupler and a particular embodiment of a force application element.

Figure 9 is a drawing showing a particular embodiment of the invention being positioned within the nostril of an equid.

Figure 10 is a drawing showing a particular embodiment of the invention being positioned within the nasal passage of an equid.

Figure 11 is a drawing showing a particular embodiment of the invention positioned within the nasal passage of an equid by comparing the location of a dose-location coordinate element with an external portion of the nostril.

#### V. MODE(S) FOR CARRYING OUT THE INVENTION

Specifically, the invention addresses apparatus and methods for the intranasal delivery of various compositions to equids. The basic technology may, however, have various applications in the medical or veterinary fields, for example, the invention may address the difficulties of delivering various compositions, including prophylactics or therapeutics, to a variety of targets susceptible to such variety of compositions in both humans and animals. The invention also provides both apparatus and methods for the

effective delivery of a wide variety of compositions which may have application in numerous other settings, including commercial production facilities, research laboratories, medical or veterinary practices, or by individual consumers.

As can be easily understood, the basic concepts of the present invention may be embodied in a variety of ways. The invention involves both methods as well as apparatus to accomplish the appropriate methods. In this application, the methods are disclosed as part of the results shown to be achieved by the various apparatus described, and as steps which are inherent to utilization. They are simply the natural result of utilizing the apparatus or devices as intended or described. In addition, while some particular embodiments of the invention are disclosed to accomplish certain methods described, it would be understood that these can be varied in a number of ways. Importantly, as to all of the foregoing, all of these facets should be understood to be encompassed by this disclosure.

The components which make up the intranasal delivery system invention are first described. Figures 1 through 8 show a particular embodiment of the intranasal delivery system invention and is but one example of the delivery system invention as described. A dose administrator (1) assists the delivery of a "dose" to a desired "target". A dose may be any desired amount of a composition or desired amount of a combination of compositions. A dose does not necessarily have to be a medicament or be used to treat humans or animals. However, a dose may include prophylactic compositions such as vaccines or therapeutic compositions such as drugs or other compositions which are of research or medicinal interest such as proteins, nucleic acids, immunogens, live or inactivated viruses, reassortant live viruses, cold-adapted live viruses, attenuated live viruses, adjuvants, or may be other substances which are useful for the delivery of or effectiveness of such compositions. The dose may also be species specific compositions such as cold-adapted live equine influenza viruses which replicate only within a certain temperature range (such as from about 26°C to about 30°C in embryonated chicken eggs), or an cold-adapted live equine influenza virus which does not form plaques in tissue culture cells at a temperature above a certain range (such as above about 37°C or above about 39°C), or an cold-adapted live equine virus having a phenotype wherein protein synthesis is inhibited above about 39°C, or an equine cold-adapted live virus having a dominant interference phenotype, as examples in the equine field. More specifically, the dose may be particular strains of virus, such as those disclosed by United States Patent Application No. 09/133,921, hereby incorporated by reference,

including equine influenza cold-adapted live viruses derived from strain A/equine/  
Kentucky/1/91 (H3N8); or EIV-P821(identified by accession No. ATCC VR 2625), EIV-  
P824 (identified by accession No. ATCC VR 2624), MSV+5(identified by accession No.  
2627); or any progeny of any of said equine influenza viruses identified by such accession  
5 Nos.; or any EIV having the identifying characteristics of such ATCC VR strains.

In general, a target to which the dose is delivered may include any desired location  
on any substrate. It may also include locations of anatomical designation both external or  
internal with respect to both humans and animals. The target may include gross anatomical  
features such as the mouth, eyes, ears, nose, genitals, or rectum, for example, or the target  
10 may be specific systems such as the central nervous system, the circulatory system or  
respiratory system, or the target may also include specific organs, tissues, cells, or other  
molecular structures associated with such gross anatomical features, systems, specific  
organs, tissues or cells. Specifically, as shown in Figures 9, 10, and 11, the target may be  
the nasal mucosa of the upper respiratory tract of an equid. Additionally, the target may be  
15 a location having specific attributes, such as a specific temperature, which makes the  
composition upon delivery more effective. For example, such specific temperature or other  
attributes may be important in promoting the replication of certain cold-adapted live viruses  
or other attribute-adapted viruses.

The dose administrator (1) may be a flexible material or a substantially rigid material  
20 depending on the application or anatomical characteristics of the species which it is designed  
to be used with. For example, a substantially rigid material may be selected for use with  
humans or bovine which may have a relatively short and uncomplicated intranasal passages  
to traverse in order to deliver the dose to the target or dose-location coordinate. Alternately,  
a more flexible dose administrator may be selected for use with equids which have longer  
25 intranasal passages to transverse and which may also have a blind-ending nasal passage  
(such as a nasal diverticulum) which may have to be worked around to deliver a dose to the  
desired target or dose location-coordinate.

The exterior configuration of the dose administrator may vary substantially in shape  
for delivery of compositions from application to application and may include, for example,  
30 cylindrical or conical configurations. As shown in Figure 1, a dose administrator may have  
a substantially uniform cylindrical exterior. The length of the dose administrator may vary  
depending on the location of the target. For applications with equids which have longer

nasal passages a cylindrical exterior surface having a radius in the range of about 1.5 millimeters (about 1/16 inch) to about 10 millimeters (about 0.4 inches), and a longitudinal length in the range of about 76 millimeters (about 3 inches) to about 180 millimeters (about 7 inches) may be appropriate. One particular embodiment of the flexible dose administrator  
5 shown by Figure 1 has a cylindrical exterior surface of about 6.5 millimeters (about 0.25 inches) and a longitudinal length of about 150 millimeters (about 5.9 inches).

The material from which the dose administrator is made may also be compatible with the composition which the dose administrator will deliver such that the dose administrator may not be degraded or so that the composition of the dose may not be altered as, for  
10 example, by heat, light, ultraviolet radiation and the like. A material suitable for the intranasal delivery of many of the above mentioned doses may be glass, polyethylene, polypropylene, polyurethane, or polyvinyl chloride.

An axial collapse prevention element (2) may be coupled to the dose administrator. The axial collapse prevention element prevents excessive axial deflection of flexible dose  
15 administrators. Excessive axial deflection may prevent the dose administrator from being properly oriented in relation to the target. The axial collapse prevention element may comprise annular or longitudinal projecting surface(s) or a pattern formed on the exterior or interior surface of the dose administrator which provides additional axial resiliency, or may comprise fibers or strands of flexibly resilient material embedded in the material from which  
20 the dose administrator is made, or may be a flexibly resilient layer responsive to the exterior cylindrical surface of the dose administrator as shown in Figure 1, although more than one layer may be used in some applications or with some types of doses. Specifically for applications with equids, a flexibly resilient layer of polyvinyl chloride or polyurethane, which may be a medical grade, having a thickness of about 1.5 millimeters (about 1/16 inch)  
25 may be used. The axial collapse prevention element (2) and the dose administrator (1) may have a unitized construction as shown in Figure 1.

To assure that the dose is delivered to the desired target a dose-location coordinate indicator (3) may be coupled to the exterior of the dose administrator. The dose-location coordinate indicator may be a visually enhanced surface such as a mark, an annular  
30 projection as shown in Figure 1, or any other element which permits location identification.

The dose-location coordinate indicator may be positioned on the dose administrator such that when aligned with a particular stop element or anatomical feature the user may be

assured that the dose is coordinated for subsequent delivery with a location which has a target susceptible to the dose (dose-location coordinate). This feature may be particularly useful when the dose administer is used to deliver a dose to a location that cannot be viewed directly. With respect to doses which are attribute or temperature sensitive the dose-location coordinate indicator may be positioned such that a dose-location coordinate has that particular attribute or temperature associated with it. For example, a dose-location coordinate indicator positioned to assure that a dose is delivered to the corresponding dose-location coordinate in the upper respiratory system of an equid having a temperature of between about 26° C to about 34° C may be essential to a virus cold-adapted to this temperature range. Specifically, with regard to particular equine applications involving the delivery of cold-adapted equine influenza virus the position of the dose-location coordinate indicator may be located at about 127 millimeters (five inches) to about 152 millimeters (six inches) from the delivery end or first end of the flexible dose administrator. This position can assure that the dose (such as a cold-adapted equine influenza virus) is delivered to a dose-location coordinate having a temperature at which replication can occur (about 26° C to about 34° C) and having mucosal cells which are susceptible to the dose. Naturally, for each application the dose-location coordinate should be affirmatively determined and the dose-location coordinate indicator positioned accordingly. The dose-location coordinate indicator and the dose administrator may also be of unitized construction.

An intranasal probe (4) may be responsive to a first end of the dose administrator. The intranasal probe can provide a surface on which a variety of dose delivery aperture elements, force dissemination contact surfaces, or an intranasal probe coupler may be attached. The dose delivery aperture element (5) may be a separate component having an aperture which penetrates the dose delivery aperture element. In that case, the dose delivery aperture element can be coupled to the intranasal probe which holds the aperture adjacent to the dose delivery administrator. Alternately the intranasal probe and the dose delivery aperture may be unitized. The aperture which penetrates the dose delivery aperture element may be further fitted with components which regulate the pressure, particle size, or the rate of delivery of the dose. A stream delivery element (6) may be coupled to the aperture, as shown in Figures 2, 4 or 6, to prevent the dose from being delivered as discrete particles but rather delivered as substantially continuous concentrated stream. The stream may be delivered with a pressure sufficient to propel the dose to the proper dose-location coordinate.

Alternately, the aperture may be fitted with other elements which deliver the dose as a fine mist, course spray, or for topical application. For equine intranasal use, the stream delivery element (6) may have an orifice of about 0.75 millimeters (about 0.030 inches).

A force dissemination contact surface (7) having hebetated termini may be coupled to the intranasal probe as shown in Figures 1, 2, 4, or 6. A purpose of the force dissemination surface may be to spread the forces from incidental contact of the dose administrator with other surfaces as the dose administrator is moved into position to deliver the dose to the proper dose-location coordinate. Spreading such forces from incidental contact may be important to prevent damage or injury to these surfaces. With respect to movement of the dose administrator into and out of anatomical passages, such as the intranasal passages, the force dissemination contact surface may prevent cutting, scoring or abrading of the tissue and minimize physical stimulation. For equine intranasal applications, a sphere cap having a radius of about 3 millimeters (about 0.125 inches) and a sphere cap height of about 1 millimeter (about 0.04 inches) may be used alone or in conjunction with a dose administrator having a cylindrical exterior surface with a radius of about 3 millimeters (about 0.125 inches) such that the force dissemination contact surface and the cylindrical exterior surface are contiguous.

An intranasal probe coupler (8) may be affixed to the intranasal probe (4). The first end of the intranasal probe coupler is responsive to the intranasal probe (4) while the second end is responsive to the dose administrator (1). At least one aperture communicates with the interior of the dose administrator and the dose delivery aperture element. The second end of the intranasal probe coupler may be responsive to either the exterior surface or the interior surface of the intranasal probe. As shown in Figures 1, 4, or 6, the second end may comprise an annular barb (9) engaged to the interior cylindrical surface of the flexible dose administrator.

The intranasal probe (4), the intranasal probe coupler (8), the force dissemination surface (7), the dose delivery aperture (5), and the stream delivery element (6) may be unitized as a single component, as shown by Figure 6, or unitized in combination with the dose administrator (1) or may be unitized in various combinations and permutations depending on the particular application.

A conformable dose sequestration element (10) may communicate with the dose delivery aperture (5). The conformable dose sequestration element may provide a dose

sequestration volume sufficiently large to contain or sequester at least one of the above-mentioned doses, either dry or combined with a diluent, such that the dose may be held separate from other components of the delivery system. The dose sequestration volume may also conform to any shape which may be desirable and may be located within the dose administrator as shown by Figures 1, 4, or 7. With respect to some applications, the conformable dose sequestration element may comprise a penetrable membrane which separates the dose from the remaining volume of the dose administrator. The conformable dose sequestration element may also be configured without a penetrable membrane. In that case the dose sequestration volume may communicate with other components of the delivery system through at least one aperture. As shown by Figure 1, the conformable dose sequestration element (10) may comprise a portion or all of the interior volume of the flexible dose administrator (1). It may be understood that the exterior surface of or the interior volume of the dose administrator may not be of uniform configuration (Figure 1 shows a generally uniform cylindrical configuration). The dose sequestration element may conform to any portion or all of such non-uniform configuration of the dose administrator. Alternately, the dose sequestration element may be a separate component made responsive to the dose delivery aperture during delivery of the dose to the dose-location coordinate.

The conformable dose sequestration element may also feature a dose retainer (11) located proximate to the dose delivery aperture (5) so as to retain the dose within the dose sequestration volume proximate to the dose delivery aperture. For some applications, this may comprise a penetrable membrane. In other applications, the conformable dose sequestration element may be configured to hold the dose adjacent to the dose delivery aperture. As shown by Figures 1, 4, or 7, the conformable dose sequestration element may be configured as a capillary which may hold the dose combined with a diluent proximate or adjacent to the dose delivery aperture in part or in whole by capillary forces. Such a capillary may be about 3 millimeters (about 1/8 inch) as shown in Figure 1. The capillary, as can be understood, may be smaller or larger as the application requires.

As such, the conformable dose sequestration element (10), the dose retainer (11), the dose administrator (1), and the axial collapse prevention element may have unitized construction or may be unitized in various combinations or permutations as certain applications require.

The conformable dose sequestration element (10) sequestering the dose may be



separated from a force application element (12) with a volume of fluid dose propellant (13). The fluid dose propellant may be a gas such as air or may be liquid such as water or a saline solution or may contain other compositions which enhance either the dose or the delivery of the dose. The fluid dose propellant may have a volume which is equal to or greater than  
5 the dead volume of the dose delivery system. This amount of fluid dose propellant may be at least the minimum volume which will deliver the entire dose when acted upon by the force application element (minimum dose delivery volume). The volume of fluid dose propellant may have a volume greater than the minimum dose delivery volume. Such volume greater than the minimum dose delivery volume, when acted upon by the force  
10 application element, can expel the dose from the dose administrator or conformable dose sequestration element and then chase the dose with the remaining portion of fluid dose propellant which exceeds the minimum dose delivery volume. Chasing the dose with the remaining portion of the fluid dose propellant can assure that substantially the entire dose may be delivered to the dose-location coordinate. As shown by Figure 1, the minimum  
15 delivery volume may about 1 to about 1.5 milliliters which may be chased with a remaining portion of fluid dose propellant as desired.

A fluid dose propellant coupler (14) may be used to couple the dose administrator (1) to the force application element (12). As shown in Figures 1, 7, or 8, the first end of the fluid dose propellant coupler may comprise an annular barb (15) responsive to the interior  
20 surface of a flexible dose administrator. The second end of the fluid dose propellant coupler may comprise a syringe adaptor. The syringe adaptor may be a leur-lock to positively lock a syringe or other force application element to the dose administrator. As shown in Figure 1 or 8, the fluid dose propellant coupler (14) and the dose-location coordinate indicator (3) may have unitized construction.

25 The force application element (12) may be responsive to the second end of the dose administrator (1) or may be coupled to the fluid dose propellant coupler (14) as above mentioned. The force application element may be any component or substance which provides sufficient force to expel the dose from the dose administrator (1) or the conformable dose sequestration element (10) to the dose-location coordinate. As shown in  
30 Figures 7 or 8, the force application element may be a plunger type syringe which could be of any size which the user finds practical or the application requires. Alternately, the force application element may be a mechanical bellows, a squeeze type bottle, compressed gas,

a liquid under pressure or otherwise as would be readily understood by those with skill in the dose delivery field.

The force application element (12) may have unitized construction with the dose administrator (1), the intranasal probe (4), the conformable dose sequestration element (10), the force dissemination contact surface (7), the dose delivery aperture (5), the stream delivery aperture (6), the axial collapse prevention element (2), or the dose-location coordinate element (3), or any of these elements in certain combinations or permutations.

An intranasal delivery system as described above may be produced by first providing a dose delivery aperture element (5) and providing a stream delivery element (6) if stream delivery of the dose to the target is desirable. If so the stream delivery aperture can be affixed to the dose delivery aperture. The next step involves coupling an intranasal probe (4) to the dose delivery aperture and thereafter coupling a force dissemination contact surface (7) having hebetated termini to the intranasal probe. Coupling an intranasal probe coupler (8) to the intranasal probe may be required for joining the dose administrator.

Assembly of these parts may be accomplished with standard fasteners, with mated surfaces, by bonding with a solvent, by friction fit, or otherwise. Naturally, these steps may be incorporated into unitized construction as shown in Figure 6 and may not comprise additional discrete steps of assembly. Joining the dose administrator (1) can comprise engaging the interior of dose administrator (1) with the intranasal probe coupler (8) which may have an annular barb (9) to secure the dose administrator to the intranasal probe. Alternately the intranasal probe may be secured to the exterior surface of the dose administrator with mated surfaces such as threads, by friction fit or by bonding the surfaces together with a solvent. The configuration of the conformable dose sequestration element (10) can be selected to have a volume which will sequester at least one dose and is compatible with the configuration of the dose administrator. The conformable dose sequestration element (10) can be coupled to the dose administrator (1) if it is not of unitary construction with the dose administrator as shown by Figure 1. Joining the axial collapse prevention element to the dose administrator (2) may comprise the bonding of discrete components annularly or longitudinally to the dose administrator but these steps may be accomplished in the design of a unitary construct comprising the dose administrator (1), conformable dose sequestration element (10), and the axial collapse prevention element (2) thereby eliminating additional discrete production steps. Positioning of the dose-location

coordinate indicator (3) at a location on the dose administrator may comprise molding a visually enhanced surface onto the dose administrator or the fluid dose propellant coupler such as a mark, a projecting surface, a recessed surface, or an annular projection as part of a unitized construct similar to that shown in Figures 1, 3, 7, or 8. Alternately, it may  
5 comprise affixing such visually enhanced surfaces, or adhesive backed label, or printed graphic to the proper location on the exterior surface of the dose administrator or the fluid dose propellant coupler as a discrete assembly step. The dose administrator (1) may be joined directly to the force application element (12) by slip fit, friction fit, or by mated surfaces such as threads or leur-lock or other engaging or locking devices. Alternately as  
10 shown by Figures 1, 3, 7, or 8 the dose administrator (1) and the force application element (12) may be joined by a dose propellant coupler which has a first end configured to engage either the interior or exterior surface of the dose administrator.

The dose delivery system as described above may be used to deliver a variety of compositions to both humans and animals including various doses intranasally. As shown  
15 by Figures 9, 10, or 11, for example, the intranasal delivery system may be used to deliver such variety of compositions to equids, humans, or other animals intranasally. In one embodiment of the invention, a dose as described above may be first sequestered within a conformable dose sequestration element (10) which separates the dose from the force application element (12) with a volume of fluid dose propellant (13). The dose may be  
20 sequestered as a substantially dry composition within the conformable dose sequestration element (10) or may be a substantially dry composition in a separate container. Establishing at least one dose in a volume of diluent can be accomplished by either combining the diluent to the dry dose in the separate container or by submerging the dose delivery aperture (5) into the diluent and reducing the pressure within the conformable dose sequestration element  
25 (10) thereby transferring the diluent to the conformable dose sequestration element. Alternately, the dose combined with the diluent in the separate container may be drawn into the conformable dose sequestration element in a similar fashion. Retaining the dose adjacent to the dose delivery aperture with a dose retainer (11) or capillary forces may provide more consistent delivery of the dose to the dose- coordinate location. The above  
30 procedure may be accomplished after measuring a volume of fluid dose propellant in excess of the minimum dose delivery volume. After positioning the intranasal probe within a nostril of the human or animal, such as an equid as shown by Figure 9, the intranasal probe

is positioned by sliding the intranasal probe into the nasal passage. Positioning a dose-location coordinate indicator (3) into proximity with an exterior portion of the nostril can assure a dose-location coordinate having a target that is susceptible to the dose or can assure that the dose-location coordinate has a temperature of about 26 C to about 34 C or as might  
5 be appropriate for a particular cold-adapted virus. With respect to equids, guiding the intranasal probe so as to not enter the false nostril can be also assured by observing that the dose-location coordinate indicator is in proximity with the exterior portion of the nostril. Once the intranasal probe is properly positioned at the dose-location coordinate, terminating sliding of the intranasal probe up the nostril prepares the device for the step of propelling  
10 the dose from the conformable dose sequestration element. Propelling the dose from the dose sequestration volume of the conformable dose sequestration element may be accomplished by applying force to the fluid dose propellant which is responsive to the dose. A portion of the fluid dose propellant is used for propelling the dose and delivering the dose onto the target. Chasing the dose with a remaining portion of the fluid dose propellant  
15 volume assures that the entire dose has been propelled from the dose sequestration volume and delivered to the target. Streaming the dose onto the target may be more effective when it is desirable to minimize the creation of smaller particles of the dose which may remain suspended in the respiratory volume, or distributed away from the target, for example.

Kits may be produced, assembled or commercialized from the various above  
20 mentioned elements in various combinations or permutations. For example, a lyophilized cold-adapted equine influenza virus(perhaps of the various strains above-mentioned) in an ampule, a dose administrator, and a force application element may be packaged for sale as a kit which can be convenient for the consumer. A diluent in a separate ampule may be added in a more complete kit. The various elements of the equine intranasal delivery device,  
25 which could be any of the combinations or permutations as described above, could be added as supplements to the kit. Naturally, the dose could be quite specific, such as certain strains of cold-adapted equine influenza viruses, such as those above-mentioned, may be packaged for use with many types of dose administrators and force application elements. Conversely, the delivery device could be quite specific, such as for a particular type of equid, for use  
30 with various materials, compositions, or other medicaments. As such, many kits may incorporate aspects or embodiments of the invention even though all the aspects of the kit are not produced by the same manufacturer.

It is thought that the apparatuses and methods of the embodiments of the present invention and many of its attendant advantages will be understood from the foregoing description and it will be apparent that various changes may be made in the form, construction and arrangement of the parts thereof without departing from the spirit and scope  
5 of the invention or sacrificing all of its material advantages, the form hereinbefore described being merely a preferred or exemplary embodiment thereof.

Particularly, it should be understood that as the disclosure relates to elements of the invention, the words for each element may be expressed by equivalent apparatus terms or method terms--even if only the function or result is the same. Such equivalent, broader, or  
10 even more generic terms should be considered to be encompassed in the description of each element or action. Such terms can be substituted where desired to make explicit the implicitly broad coverage to which this invention is entitled. As but one example, it should be understood that all action may be expressed as a means for taking that action or as an element which causes that action. Similarly, each physical element disclosed should be  
15 understood to encompass a disclosure of the action which that physical element facilitates.

Regarding this last aspect, and as but one example the disclosure of a "conformable dose sequestration element" should be understood to encompass disclosure of the act of "conforming a dose sequestration element"--whether explicitly discussed or not--and, conversely, were there only disclosure of the act of "conforming a dose sequestration  
20 element", such a disclosure should be understood to encompass disclosure of a "dose sequestration element". Such changes and alternative terms are to be understood to be explicitly included in the description.

Any acts of law, statutes, regulations, or rules mentioned in this application for patent; or patents, publications, or other references mentioned in this application for patent  
25 are hereby incorporated by reference. In addition, as to each term used it should be understood that unless its utilization in this application is inconsistent with such interpretation, common dictionary definitions should be understood as incorporated for each term and all definitions, alternative terms, and synonyms such as contained in the Random House Webster's Unabridged Dictionary, second edition are hereby incorporated by  
30 reference. Finally, all references listed in any information disclosure filed with and/or for the application are hereby incorporated by reference, however, as to each of the above, to the extent that such information or statements incorporated by reference might be considered

inconsistent with the patenting of this/these invention(s) such statements are expressly not to be considered as made by the applicant(s).

Further, the disclosure should be understood to include support for each feature, component, and step shown as separate and independent inventions as well as the various  
5 combinations and permutations of each.

In addition, unless the context requires otherwise, it should be understood that the term “comprise” or variations such as “comprises” or “comprising”, are intended to imply the inclusion of a stated element or step or group of elements or steps but not the exclusion of any other element or step or group of elements or steps. Such terms should be interpreted  
10 in their most expansive form so as to afford the applicant the broadest coverage legally permissible in countries such as Australia and the like. Such terms are intended to have an inclusive meaning rather than an exclusive one and should be interpreted in their most expansive form so as to afford the applicant the broadest coverage legally permissible. Therefore, in countries such as Australia and the like, such terms are not intended to have  
15 an exclusive, or more limited meaning.

Thus, the applicant(s) should be understood to claim at least: i) the delivery devices as herein disclosed and described, ii) the related methods disclosed and described, iii) similar, equivalent, and even implicit variations of each of these devices and methods, iv) those alternative designs which accomplish each of the functions shown as are disclosed and  
20 described, v) those alternative designs and methods which accomplish each of the functions shown as are implicit to accomplish that which is disclosed and described, vi) each feature, component, and step shown as separate and independent inventions, vii) the applications enhanced by the various systems or components disclosed, viii) the resulting products produced by such systems or components, and ix) methods and apparatuses substantially as  
25 described hereinbefore and with reference to any of the accompanying examples, and x) the various combinations and permutations of each of the elements disclosed.

## VI. CLAIMS

We claim:

1. An equine intranasal delivery device, comprising:
  - a. a dose delivery aperture element;
  - 5 b. an intranasal probe coupled to said dose delivery aperture element;
  - c. a force dissemination contact surface having hebetated termini responsive to said intranasal probe;
  - d. a flexible dose administrator having a first end and a second end, wherein said first end is coupled to said intranasal probe; and
  - 10 e. a conformable dose sequestration element having a dose sequestration volume sufficiently large to sequester a dose which communicates with said dose delivery aperture element.
2. An equine intranasal delivery device as described in claim 1, further comprising a force application element coupled to said second end of said flexible dose administrator.
- 15 3. An equine intranasal delivery device as described in claim 2, further comprising a fluid dose propellant which separates said conformable dose sequestration element from said force application element.
4. An equine intranasal delivery device as described in claim 3, wherein said fluid dose propellant has a volume greater than a minimum dose delivery volume.
- 20 5. An equine intranasal delivery device as described in claim 4, wherein said fluid dose propellant has a volume between about 1 milliliters to about 5 milliliters.
6. An equine intranasal delivery device as described in claim 5, wherein said fluid dose propellant is selected from a group consisting of: a liquid, a diluent, water, a saline solution, or air.
- 25

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7. An equine intranasal delivery device as described in claim 6, wherein said conformable dose sequestration element further comprises a dose retainer located adjacent to said dose delivery aperture element.
  8. An equine intranasal delivery device as described in claim 7, wherein said dose  
5 retainer is a capillary.
  9. An equine intranasal delivery device as described in claim 8, wherein said capillary has a diameter of about 3 millimeters ( about 0.125 inches).
  10. An equine intranasal delivery device as described in claim 9, further comprising a  
10 stream delivery element coupled to said dose delivery aperture element.
  11. An equine intranasal delivery device as described in claim 10, wherein said stream delivery element has a diameter of about 0.75 millimeters (about 0.030 inches).
  12. An equine intranasal delivery device as described in claim 11, wherein said flexible  
15 dose administrator has a cylindrical exterior surface having a radius of about 3 millimeters (about 0.125 inches).
  13. An equine intranasal delivery device as described in claim 12, wherein said cylindrical exterior surface has longitudinal length of about 150 millimeters (about 5.9 inches).
  14. An equine intranasal delivery device as described in claim 13, wherein said force  
20 dissemination contact surface comprises a sphere cap having a radius of about 3 millimeters (about 0.125 inches) and wherein said sphere cap has a height of about 1 millimeter (about 0.04 inches).
  15. An equine intranasal delivery device as described in claim 14, wherein said sphere cap and said cylindrical exterior surface are contiguous.



16. An equine intranasal delivery device as described in claim 1, further comprising a dose-location coordinate indicator coupled to said flexible dose administrator.
17. An equine intranasal delivery device as described in claim 16, wherein said dose-location coordinate indicator comprises a visually enhanced surface coupled to said exterior surface of said flexible dose administrator.
18. An equine intranasal delivery device as described in claim 17, wherein said visually enhanced surface coupled to an exterior surface of said flexible dose administrator comprises an annular projection.
19. An equine intranasal delivery device as described in claim 18, wherein said dose-location coordinate indicator has a position which assures a dose-location coordinate temperature between about 26° C to about 34° C.
20. An equine intranasal delivery device as described in claim 19, wherein said dose-location coordinate indicator has a position at about 150 millimeters (about 5.9 inches) from said dose delivery aperture.
21. An equine intranasal delivery device as described in claim 1, further comprising an axial collapse prevention element coupled to said flexible dose administrator.
22. An equine intranasal delivery device as described in claim 21, wherein said axial collapse prevention element comprises a flexibly resilient layer between said exterior cylindrical surface of said flexible dose administrator and said conformable dose sequestration element.
23. An equine intranasal delivery device as described in claim 22, wherein said flexibly resilient layer comprises polyvinyl chloride having a thickness of 1.5 millimeters (about 0.060 inches).

24. An equine intranasal delivery device as described in claim 1, further comprising an intranasal probe coupler having a first end responsive to said intranasal probe and a second end responsive to said flexible dose administrator, wherein said intranasal probe coupler has at least one aperture which communicates between said volume of said conformable dose sequestration element and said dose delivery aperture element.
25. An equine intranasal delivery device as described in claim 24, wherein said second end of said intranasal probe coupler comprises an annular barb engaged to an interior cylindrical surface of said flexible dose administrator.
26. An equine intranasal delivery device as described in claim 25, further comprising a fluid dose propellant coupler having a first end responsive to said interior cylindrical surface of said flexible dose administrator and a second end responsive to said fluid dose propellant, wherein said fluid dose propellant coupler has at least one aperture which communicates between said volume of said conformable dose sequestration element and said fluid dose propellant.
27. An equine intranasal delivery device as described in claim 26, wherein said first end of said fluid dose propellant coupler comprises an annular barb engaged to said interior cylindrical surface of said flexible dose administrator.
28. An equine intranasal delivery device as described in claim 27, wherein said second end of said fluid dose propellant coupler comprises a syringe adaptor.
29. An equine intranasal delivery device as described in claim 28, wherein said syringe adaptor is a luer-lock.
30. An equine intranasal delivery device as described in claim 29, wherein said force application element is a syringe.
31. An equine intranasal delivery device as described in claim 24, wherein said

intranasal probe and said intranasal probe coupler have unitized construction.

32. An equine intranasal delivery device as described in claim 24, wherein said intranasal probe, said intranasal probe coupler, and said force dissemination contact surface having hebetated termini have unitized construction.
- 5 33. An equine intranasal delivery device as described in claim 1, wherein said flexible dose administrator and said conformable dose sequestration element have unitized construction.
34. An equine intranasal delivery device as described in claim 22, wherein said flexible dose administrator, said conformable dose sequestration element, and said axial collapse protection element have unitized construction.
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35. An equine intranasal delivery device as described in claim 24, wherein said intranasal probe, said intranasal probe coupler, said force dissemination contact surface having hebetated termini, said flexible dose administrator, said conformable dose sequestration element, and said axial collapse protection element have unitized construction.
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36. An equine intranasal delivery device as described in claim 26, wherein said fluid dose propellant coupler and said dose-location coordinate indicator have unitized construction.
- 20 37. An equine intranasal delivery device as described in claim 1, further comprising a dose responsive to said conformable dose sequestration element.
38. An equine intranasal delivery device as described in claim <sup>37</sup>36, wherein said dose comprises a material selected from the group consisting of: a substance, a composition, a therapeutic composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen which elicits an immune response, a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated
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- live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26°C to about 30°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39°C, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39°C, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No. 2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.
39. An equine intranasal delivery device as described in claim 38, further comprising dose diluent, wherein said dose and said dose diluent are combined.
40. An equine intranasal delivery device as described in claim 39, wherein said dose diluent has a volume of about 0.5 milliliters to about 1.5 milliliters.
41. An equine intranasal delivery device as described in claim 1, further comprising an equid.
42. A kit for intranasal delivery, comprising:
- a. a dose;
  - b. a diluent in which said dose may be combined; and
  - c. an intranasal device comprising:
    - i. an intranasal probe having a dose delivery aperture;
    - ii. a dose administrator having a first end and a second end, wherein said first end is responsive to said intranasal probe; and

- iii. an intranasal probe coupler responsive to said intranasal probe and said first end of said dose administrator, wherein said intranasal probe coupler has at least one aperture which communicates between said dose administrator and said intranasal probe.

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43. An intranasal delivery device as described in claim 42, further comprising a force application element coupled to said second end of said flexible dose administrator.
44. An intranasal delivery device as described in claim 42, wherein said dose comprises a material selected from the group consisting of: an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26°C to about 30°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39°C, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39°C, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No.2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about 10<sup>5</sup> TCID<sub>50</sub> to about 10<sup>8</sup> TCID<sub>50</sub> units.
45. An equine intranasal delivery device as described in claim 43, wherein said force application element is a syringe.
46. An intranasal delivery device as described in claim 45, wherein said dose administrator comprises a flexible material.
47. An intranasal delivery device as described in claim 42, further comprising a dose-

location coordinate indicator responsive to said flexible dose administrator.

48. An equine intranasal delivery device as described in claim 47, wherein said dose-location coordinate indicator has a position which assures a dose-location coordinate temperature between about 26° C to about 34° C.
- 5 49. An intranasal delivery device as described in claim 42, further comprising a force dissemination contact surface having hebetated termini responsive to said exterior surface of said intranasal probe.
50. An intranasal delivery device as described in claim 42, further comprising a conformable dose sequestration element having a dose sequestration volume  
10 sufficient to sequester said dose.
51. An intranasal delivery device as described in claim 50, wherein said conformable dose sequestration element further comprises a dose retainer, wherein said dose retainer positions said dose proximate to said dose delivery aperture.
52. An intranasal delivery device as described in claim 42, further comprising a stream  
15 delivery element coupled to said dose delivery aperture.
53. An equine intranasal delivery device, comprising:  
a. a dose administrator;  
b. a force application element coupled to said dose administrator; and  
c. a an equine influenza cold-adapted live virus derived from strain A/equine/  
20 Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No.2627) dose responsive to said force application element.
54. An equine intranasal delivery device as described in claim 53, further comprising a  
25 dose diluent, wherein said dose and said dose diluent are combined.

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55. An equine intranasal delivery device as described in claim 54, wherein said force application element is a syringe.
56. An equine intranasal delivery device as described in claim 55, further comprising a coupler element having a first end responsive to said dose administrator and a second end responsive to said force application element, wherein said coupler element has at least one aperture which communicates between a volume of said dose administrator and said force application element.
57. An equine intranasal delivery device as described in claim 56, further comprising an intranasal probe coupled to said dose administrator.
58. An equine intranasal delivery device as described in claim 57, further comprising an intranasal probe coupler having a first end responsive to said intranasal probe and a second end responsive to said dose administrator, wherein said intranasal probe coupler has at least one aperture which communicates between said volume of said dose administrator and an exterior surface of said intranasal probe.
59. An equine intranasal delivery device as described in claim 58, wherein said dose administrator comprises a flexible material.
60. An intranasal delivery device, comprising:
- a. a dose administrator;
  - b. a force application element coupled to said dose administrator; and
  - c. a dose responsive to said force application element.
61. An intranasal delivery device as described in claim 60, further comprising a dose diluent, wherein said dose and said dose diluent are combined.
62. An intranasal delivery device as described in claim 61, wherein said force application element is a syringe.

63. An intranasal delivery device as described in claim 62, further comprising a coupler element having a first end responsive to said dose administrator and a second end responsive to said force application element, wherein said coupler element has at least one aperture which communicates between a volume of said dose administrator and said force application element.
64. An intranasal delivery device as described in claim 63, further comprising an intranasal probe coupled to said dose administrator.
65. An intranasal delivery device as described in claim 64, further comprising an intranasal probe coupler having a first end responsive to said intranasal probe and a second end responsive to said dose administrator, wherein said intranasal probe coupler has at least one aperture which communicates between said volume of said dose administrator and an exterior surface of said intranasal probe.
66. An intranasal delivery device as described in claim 65, wherein said dose administrator comprises a flexible material.
67. An intranasal delivery device as described in any one of claims 60, wherein said dose comprises a material selected from the group consisting of: an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26°C to about 30°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39°C, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39°C, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No. 2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said



ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.

68. A method for producing an equine intranasal delivery device, comprising the steps of:
- 5 a. providing a dose delivery aperture element;
- b. coupling an intranasal probe to said dose delivery aperture;
- c. joining a flexible dose administrator having a first end and a second end to said intranasal probe by said first end; and
- 10 d. coupling a conformable dose sequestration element having a dose sequestration volume which communicates with said dose delivery aperture element.
69. A method for producing an equine intranasal delivery device as described in claim 68, further comprising the step of coupling a force application element to said fluid dose propellant.
- 15 70. A method for producing an equine intranasal delivery device as described in claim 69, further comprising the step of separating said conformable dose sequestration element having a dose sequestration volume from said force application element with a fluid dose propellant.
- 20 71. A method for producing an equine intranasal delivery device as described in claim 60, further comprising the step of coupling a force dissemination contact surface having hebetated termini to said intranasal probe.
72. A method for producing an equine intranasal delivery device as described in claim 61, further comprising the step of providing a stream delivery element.
- 25 73. A method for producing an equine intranasal delivery device as described in claim 62, further comprising the step of positioning a dose-location coordinate indicator at a location on said flexible dose administrator, wherein said location of said dose-

location coordinate indicator assures delivery of said dose to a target which is susceptible to said dose.

74. A method for producing an equine intranasal delivery device as described in claim 73, further comprising the step of joining an axial collapse protection element coupled to said flexible dose administrator.

75. A method for producing an equine intranasal delivery device as described in claim 74, further comprising coupling an intranasal probe coupler to said intranasal probe and to said flexible dose administrator, wherein said intranasal probe coupler has at least one aperture which communicates between said volume of said conformable dose sequestration element and said dose delivery aperture.

76. A method for producing an equine intranasal delivery device as described in claim 75, further comprising the step of coupling a fluid dose propellant coupler to said conformable dose sequestration element and to said dose propellant, wherein said fluid dose propellant coupler has at least one aperture which communicates between said volume of said conformable dose sequestration element and said fluid dose propellant.

77. A method for producing an equine intranasal delivery device as described in claim 76, further comprising the step of selecting a dose from the group consisting of: a substance, a composition, a therapeutic composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen which elicits an immune response, a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26°C to about 30°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39°C, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39°C, an equine cold-adapted

live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821 (identified by accession No. ATCC VR2625), EIV-P824 (identified by accession No. ATCC VR2624), MSV+5 (identified by accession No. 2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^6$  TCID<sub>50</sub> units.

78. A method for producing an equine intranasal delivery device as described in claim 77, further comprising the step of sequestering a dose within said dose sequestration volume of said conformable dose sequestration element.

79. A method for producing an equine intranasal delivery device as described in claim 78, wherein said step of sequestering said dose within said volume of said conformable dose sequestration element further comprises:

- a. establishing a volume of diluent containing said dose within said volume of said conformable dose sequestration element;
- b. removing said volume of diluent from said dose; and
- c. leaving a dry dose within said dose sequestration volume of said conformable dose sequestration element.

80. A method for producing an equine intranasal delivery device as described in claim 78, wherein said step of sequestering said dose within said interior volume of said flexible dose sequestration element further comprises:

- a. establishing a volume of diluent containing said dose within said volume of said conformable dose sequestration element;
- b. establishing conditions within said volume of diluent containing said dose wherein said dose does not substantially degrade.

81. A method of equine intranasal delivery, comprising the steps of:

- a. sequestering a dose within a conformable dose sequestration element,

- wherein said conformable dose sequestration element separates said dose from a force application element with a volume of a fluid dose propellant;
- b. positioning an intranasal probe within a nostril of an equid;
  - c. sliding said intranasal probe up said nostril of said equid;
  - 5 d. terminating sliding of said intranasal probe up said nostril;
  - e. propelling said dose from said conformable dose sequestration element; and
  - f. delivering said dose onto a target of said equid.
82. A method of intranasal delivery as described in claim 81, wherein said step of delivering said dose onto said target of said equid comprises streaming said dose
- 10 onto said target of said equid.
83. A method of intranasal delivery as described in claim 82, wherein said step of sequestering a dose within a conformable dose sequestration element, further comprises the steps of:
- a. establishing at least one dose in a volume of diluent;
  - 15 b. submerging said dose delivery aperture into said volume of diluent containing at least one dose; and
  - c. reducing pressure within said conformable dose sequestration element sufficient to transfer said dose established in said volume of diluent into said conformable dose sequestration element.
- 20 84. A method of intranasal delivery as described in claim 83, further comprising the step of retaining said dose within said conformable dose sequestration element adjacent to said intranasal probe.
85. A method of intranasal delivery as described in claim 84, further comprising the step of guiding said intranasal probe so as to not enter an opening to a false nostril.
- 25 86. A method of intranasal delivery as described in claim 81, further comprising the step of positioning a dose-location coordinate indicator into proximity with an exterior portion of said nostril of said equid.

87. A method of intranasal delivery as described in claim 86, wherein said step of positioning a dose-location coordinate indicator into proximity with an exterior portion of said nostril of said equid assures a dose-location coordinate having a temperature of about 26°C to about 34°C
- 5 88. A method of intranasal delivery as described in any one of claims 87, wherein said step of propelling said dose from said conformable dose sequestration element further comprises the steps of:
- 10 a. measuring a fluid dose propellant volume, wherein said volume of said fluid dose propellant is in excess of a volume of a minimum dose delivery volume;
- b. propelling said dose from said volume of said conformable dose sequestration element with a portion of said dose propellant volume; and
- c. chasing said dose with a remaining portion of said dose propellant volume.
- 15 89. An equine intranasal delivery device as described in claim 88, wherein said dose comprises a substance selected from the group consisting of: a substance, a composition, a therapeutic composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen which elicits an immune response, a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in
- 20 embryonated chicken eggs within a temperature range from about 26°C to about 30°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39°C, a equine cold-adapted live virus having a phenotype
- 25 wherein protein synthesis is inhibited above about 39°C, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No.2627), any
- 30 progeny of any of said equine influenza viruses identified by such accession Nos.,

any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.

90. An intranasal delivery device, comprising:
- 5 a. a force application element;
- b. a conformable dose sequestration element having a dose sequestration volume sufficiently large to sequester a dose, wherein said conformable dose sequestration element separates said dose from said force application element; and
- 10 c. a fluid dose propellant which separates said conformable dose sequestration element from said force application element.
91. An intranasal delivery device as described in claim 90, further comprising an intranasal probe responsive to said conformable dose sequestration element.
- 15 92. An intranasal delivery device as described in claim 91, further comprising a dose delivery aperture element coupled to said intranasal probe.
93. An intranasal delivery device as described in claim 92, further comprising a stream delivery element coupled to said dose delivery aperture element.
- 20 94. An intranasal delivery device as described in claim 93, wherein said stream delivery element has a diameter of about 0.75 millimeters (about 0.030 inches).
95. An intranasal delivery device as described in claim 94, further comprising a flexible dose administrator having a cylindrical exterior surface.
- 25 96. An intranasal delivery device as described in claim 95, wherein said cylindrical exterior surface of said flexible dose administrator has a radius of 3 millimeters (about 0.125 inches).

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97. An intranasal delivery device as described in claim 96, wherein said cylindrical exterior surface of said flexible administrator has a length of about 150 millimeters (about 5.9 inches).
- 5 98. An intranasal delivery device as described in claim 97, further comprising a force dissemination contact surface having hebetated termini responsive to said intranasal probe.
- 10 99. An intranasal delivery device as described in claim 98, wherein said force dissemination contact surface responsive to said intranasal probe comprises a sphere cap wherein said sphere cap and a cylindrical exterior surface of said flexible dose administrator form a contiguous surface.
100. An intranasal delivery device as described in claim 99, wherein said sphere cap has a radius of about 3 millimeters (about 0.125 inches) and a sphere cap height of about 1 millimeters (about 0.040 inches) and wherein said cylindrical exterior surface has a radius of about 3 millimeters (about 0.125 inches).
- 15 101. An intranasal delivery device as described in claim 100, wherein said intranasal probe and said force dissemination contact surface have a unitized construction.
102. An intranasal delivery device as described in claim 101, wherein said conformable dose sequestration element further comprises a dose retainer, wherein said dose retainer positions said dose contained within said volume of solvent proximate to
- 20 said dose delivery aperture.
103. An intranasal delivery device as described in claim 102, wherein said dose retainer is a capillary.
104. An intranasal delivery device as described in claim 103, wherein said capillary has a diameter of about 3 millimeters (about 0.125 inches).

105. An intranasal delivery device as described in claim 104, wherein said volume of diluent is about 1 milliliter.
106. An intranasal delivery device as described in claim 105, wherein said fluid dose propellant has a volume in a range of about 1 milliliters to about 3 milliliters.
- 5 107. An intranasal delivery device as described in claim 106, further comprising a dose-location coordinate indicator coupled to said dose sequestration element.
108. An intranasal delivery device as described in claim 107, wherein said dose-location coordinate indicator comprises a visually enhanced surface coupled to said exterior surface of said dose sequestration element.
- 10 109. An intranasal delivery device as described in claim 108, wherein said visually enhanced surface coupled to said exterior surface of said dose sequestration element comprises an annular projection.
110. An equine intranasal delivery device as described in claim 119, wherein said dose-location coordinate indicator has a position which assures a dose-location coordinate  
15 temperature between about 26° C to about 34° C.
111. An intranasal delivery device as described in claim 110, wherein said dose-location coordinate indicator has a position at about 150 millimeters (about 5.9 inches) from said first end of said dose sequestration element.
- 20 112. An intranasal delivery device as described in claim 111, further comprising an axial collapse prevention element coupled to said dose sequestration element.
113. An intranasal delivery device as described in claim 112, wherein said axial collapse prevention element comprises a flexibly resilient layer between said exterior cylindrical surface of said flexible dose administrator and said volume of said  
25 conformable dose sequestration element.



114. An intranasal delivery device as described in claim 113, further comprising an intranasal probe coupler having a first end responsive to said intranasal probe and a second end responsive to said dose sequestration element, wherein said intranasal probe coupler has at least one aperture which communicates between said volume of said conformable dose sequestration element and said dose delivery aperture.
115. An intranasal delivery device as described in claim 114, wherein said second end of said intranasal probe coupler comprises an annular barb engaged to said interior surface of said conformable dose sequestration element.
116. An intranasal delivery device as described in claim 115, wherein said intranasal probe coupler and intranasal probe comprise unitized construction.
117. An intranasal delivery device as described in claim 116, wherein said intranasal probe coupler, said intranasal probe, and said force dissemination contact surface having hebetated termini comprise unitized construction.
118. An intranasal delivery device as described in claim 117, further comprising a propellant coupler having a first end responsive to said interior volume of said dose sequestration element and a second end responsive to said fluid dose propellant, wherein said propellant coupler has at least one aperture which communicates between said interior volume of said conformable dose sequestration element and said fluid dose propellant.
119. An intranasal delivery device as described in claim 118, wherein said first end of said propellant coupler comprises an annular barb engaged to said interior surface of said conformable dose sequestration element.
120. An intranasal delivery device as described in claim 119, wherein said second end of said propellant coupler comprises a syringe adaptor.
121. An intranasal delivery device as described in claim 120, wherein said syringe

adaptor comprises a leur-lock.

122. An intranasal delivery device as described in claim 121, wherein said propellant coupler, and said dose-location coordinate indicator comprise unitized construction.
123. An intranasal delivery device as described in claim 122, wherein said force application element is a syringe.
124. An equine intranasal delivery device as described in claim 123, wherein said dose comprises a substance selected from the group consisting of: a composition, a therapeutic composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen which elicits an immune response, a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26°C to about 30°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39°C, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39°C, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No. 2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.
125. An intranasal delivery device as described in claim 124, further comprising an equid.
126. A method of delivering a dose intranasally, comprising the steps of:
- sequestering a dose within an dose sequestration element, wherein said

- conformable dose sequestration element separates said dose from a force application element with a volume of a fluid dose propellant;
- b. measuring a volume of fluid dose propellant, wherein said volume is in excess of a minimum delivery volume of said dose;
- 5 c. applying force to said volume of said fluid dose propellant;
- d. propelling said dose from said interior volume of said dose sequestration element;
- e. delivering said dose to a target susceptible to said dose; and
- f. expelling a remaining portion of said volume of said fluid dose propellant
- 10 from said conformable dose sequestration element.
127. A method of intranasal delivery as described in claim 126, wherein said step of delivering said dose to said target susceptible to said dose comprises streaming said dose onto said target susceptible to said dose.
128. A method of intranasal delivery as described in claim 127, wherein said step of sequestering said dose within said interior volume of said dose sequestration element
- 15 further comprises:
- a. establishing at least one dose in a volume of diluent;
- b. submerging said dose sequestration element into said volume of solvent containing said at least one dose; and
- 20 c. reducing pressure within said volume of said conformable dose sequestration element sufficiently to transfer said dose into said interior volume of said conformable dose sequestration element.
129. A method of intranasal delivery as described in claim 128, wherein establishing said at least one dose within said volume of said conformable dose sequestration element
- 25 further comprises retaining said dose in a position by capillary forces.
130. A method of intranasal delivery as described in claim 129, further comprising the step of providing an intranasal probe responsive to said conformable dose sequestration element.

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131. A method of intranasal delivery as described in claim 130, further comprising the step of providing a flexible dose administrator responsive to said conformable dose sequestration element.
132. A method of intranasal delivery as described in claim 131, further comprising the step of sliding said intranasal probe up a nostril of an animal.
133. A method of intranasal delivery as described in claim 132, further comprising the step of guiding said intranasal probe so as to not enter an opening to a false nostril.
134. A method of intranasal delivery as described in claim 133, further comprising the step of positioning a dose-location coordinate indicator into proximity with an exterior portion of said nostril of said animal.
135. A method of intranasal delivery as described in claim 134, wherein said step of positioning a dose-location coordinate indicator into proximity with an exterior portion of said nostril of said equid assures a dose-location coordinate having a temperature of about 26°C to about 34°C
136. A method of intranasal delivery as described in claim 135, further comprising the step of terminating sliding of said intranasal probe up said nostril of said animal.
137. A method of intranasal delivery as described in claim 136, further comprising the step of administering said dose to said target of an equid.
138. An equine intranasal delivery device as described in claim 137, further comprising the step of selecting said from the group consisting of: a composition, a therapeutic composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen which elicits an immune response, a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26°C to about 30°C, an equine influenza

cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39°C, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39°C, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821 (identified by accession No. ATCC VR2625), EIV-P824 (identified by accession No. ATCC VR2526), MSV+5 (identified by accession No.2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about 10<sup>5</sup> TCID<sub>50</sub> to about 10<sup>8</sup> TCID<sub>50</sub> units.

139. An intranasal dose delivery device, comprising:
- a. a stream delivery element;
  - b. a dose delivery aperture element coupled to said stream delivery element;
  - c. an intranasal probe responsive to said dose delivery aperture;
  - d. a flexible dose administrator;
  - e. an intranasal probe coupler having a first end responsive to said intranasal probe and a second end responsive to said flexible dose administrator, wherein said intranasal probe coupler has at least one aperture which communicates between said intranasal probe and said stream delivery element;
  - f. a force application element responsive to said flexible dose administrator; and
  - g. a force application element coupler having a first end responsive to said flexible dose administrator and a second end responsive to said force application element, wherein said force application coupler has at least one aperture which communicates between said flexible dose administration element and said force application element.

140. An intranasal delivery device as described in claim 139, wherein said stream

delivery element has an aperture having a diameter of about 0.75 millimeters (about 0.030 inches).

141. An intranasal delivery device as described in claim 140, wherein said flexible dose administrator has a cylindrical exterior surface.

5 142. An intranasal delivery device as described in claim 141, wherein said cylindrical exterior surface has a diameter of about 6 millimeters (about 0.250 inches).

143. An intranasal delivery device as described in claim 142, wherein said cylindrical exterior surface has a length of about 150 millimeters (about 5.9 inches).

10 144. An intranasal delivery device as described in claim 143, further comprising a force dissemination contact surface having hebetated termini coupled to said intranasal probe.

15 145. An intranasal delivery device as described in claim 144, wherein said force dissemination contact surface responsive to said flexible intranasal probe comprises a sphere cap, wherein said sphere cap and said cylindrical exterior surface of said flexible dose administrator form a contiguous surface.

146. An intranasal delivery device as described in claim 145, wherein said sphere cap has a radius of about 3 millimeters (about 0.125 inches) and a sphere cap height of about 1 millimeters (about 0.040 inches).

20 147. An intranasal delivery device as described in claim 146, wherein said intranasal probe and said force dissemination contact surface have a unitized construction.

148. An intranasal delivery device as described in any one of claims 139 or 146, further comprising a conformable dose sequestration element having a dose sequestration volume responsive to said flexible dose administrator.

149. An intranasal delivery device as described in claim 148, wherein said conformable dose sequestration element further comprises a dose retainer, wherein said dose retainer has a location proximate to said stream delivery element.
150. An intranasal delivery device as described in claim 149, wherein said dose retainer  
5 comprises a capillary.
151. An intranasal delivery device as described in claim 150, wherein said capillary has a diameter of 3 millimeters (about 0.125 inches).
152. An intranasal delivery device as described in claim 151, further comprising an axial collapse prevention element coupled to said flexible dose administrator.
- 10 153. An intranasal delivery device as described in claim 152, wherein said axial collapse prevention element comprises a resiliently flexible layer between said cylindrical exterior surface of said flexible dose administrator and said conformable dose sequestration element.
154. An intranasal delivery device as described in claim 153, wherein said resiliently  
15 flexible layer comprises polyvinyl chloride having a thickness of about 1.5 millimeters (0.040 inches).
155. An intranasal delivery device as described in claim 154, further comprising a dose-location coordinate indicator coupled to said flexible dose administrator.
- 20 156. An intranasal delivery device as described in claim 155, wherein said dose-location coordinate indicator comprises a visually enhanced surface.
157. An intranasal delivery device as described in claim 156, wherein said visually enhanced surface comprises an annular projection.
158. An equine intranasal delivery device as described in claim 157, wherein said dose-

location coordinate indicator has a position which assures a dose-location coordinate temperature between about 26° C to about 34° C.

159. An intranasal delivery device as described in claim 158, wherein said dose-location coordinate indicator has a position on said flexible intranasal probe distal from said stream delivery element of about 150 millimeters (about 5.9 inches).
160. An intranasal delivery device as described in claim 159, further comprising a fluid dose propellant which separates said conformable dose sequestration element from said force application element.
161. An intranasal delivery device as described in claim 160, wherein said flexible dose administrator and said dose sequestration element have a unitized construction.
162. An intranasal delivery device as described in claim 161, wherein said second end of said intranasal probe coupler comprises an annular barb engaged to said interior surface of said flexible dose administrator.
163. An intranasal delivery device as described in claim 162, wherein said intranasal probe coupler and intranasal probe comprise unitized construction.
164. An intranasal delivery device as described in claim 163, wherein said intranasal probe coupler, said intranasal probe, and said force dissemination contact surface having hebetated termini comprise unitized construction.
165. An intranasal delivery device as described in claim 164, wherein said first end of said propellant coupler comprises an annular barb engaged to said interior surface of said flexible dose administrator.
166. An intranasal delivery device as described in claim 165, wherein said second end of said force application element coupler comprises a syringe adaptor.



167. An intranasal delivery device as described in claim 166, wherein said syringe adaptor comprises a leur-lock.
168. An intranasal delivery device as described in claim 167, wherein said force application element coupler and said dose-location coordinate indicator comprise unitized construction.
169. An intranasal delivery device as described in claim 168, further comprising a dose responsive to said stream delivery element.
170. An equine intranasal delivery device as described in claim 169, wherein said dose comprises a substance selected from the group consisting of: a composition, a therapeutic composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen which elicits an immune response, a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26°C to about 30°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39°C, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39°C, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No.2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.
171. An intranasal delivery device as described in claim 170, further comprising a volume of diluent, wherein said volume of diluent and said dose are combined.

172. An intranasal delivery device as described in claim 171, further comprising an equid.
173. A method of delivering a dose intranasally, comprising the steps of:
- a. establishing a dose in a volume of diluent within a flexible administrator;
  - b. positioning said flexible administrator within a nostril of an animal;
  - 5 c. applying force to said dose in said volume of diluent;
  - d. propelling said dose in said volume of diluent from a stream delivery element; and
  - e. streaming said dose in said volume of diluent onto a target susceptible to said dose.
- 10 174. A method of delivering a dose intranasally as described in claim 173, wherein steps d and e occur simultaneously.
175. A method of delivering a dose intranasally as described in claim 174, further comprising the step of providing a flexible dose administrator responsive to said intranasal probe.
- 15 176. A method of delivering a dose intranasally as described in claim 175, further comprising the step of sliding said flexible dose administrator up a nostril of an animal.
177. A method of delivering a dose intranasally as described in claim 176, further comprising the step of disseminating the force of contact between said flexible dose administrator and a nasal passage of said animal.
- 20 178. A method of delivering a dose intranasally as described in claim 177, further comprising the step of preventing axial collapse of said flexible dose administrator.
179. A method of delivering a dose intranasally as described in claim 178, further comprising the step of positioning a dose-location coordinate indicator into
- 25 proximity with an exterior portion of said nostril of said animal.

180. A method of intranasal delivery as described in claim 179, wherein said step of positioning a dose-location coordinate indicator into proximity with an exterior portion of said nostril of said equid assures a dose-location coordinate having a temperature of about 26°C to about 34°C
- 5 181. A method of delivering a dose intranasally as described in claim 180, further comprising the step of terminating sliding of said flexible dose administrator up said nostril of said animal.
- 10 182. A method of delivering a dose intranasally as described in claim 181, further comprising the step of sequestering a dose in a volume of a conformable dose sequestration element, wherein said conformable dose sequestration element separates said dose from a force application element with a volume of fluid dose propellant.
- 15 183. A method of delivering a dose intranasally as described in claim 182, further comprising the step of measuring a volume of fluid dose propellant, wherein said volume of fluid dose propellant has a volume in excess of a minimum dose delivery volume.
184. A method of delivering a dose intranasally as described in claim 183, further comprising chasing said dose with said volume in excess of said minimum dose delivery volume.
- 20 185. A method of intranasal delivery as described in claim 184, wherein said step of sequestering said dose within said interior volume of said dose sequestration element further comprises:
- a. establishing at least one dose in a volume of diluent;
  - b. submerging said conformable dose sequestration element into said volume of diluent containing said at least one dose; and
  - 25 c. reducing pressure within said volume of said conformable dose sequestration element sufficiently to transfer said dose into said dose sequestration volume

of said conformable dose sequestration element.

186. A method of intranasal delivery as described in claim 185, wherein establishing said at least one dose within said volume of said conformable dose sequestration element further comprises retaining said dose in a position proximate to said stream delivery element by capillary forces.
187. A method of intranasal delivery as described in claim 186, further comprising the step of administering said dose to an equid.
188. A method of intranasal delivery as described in claim 187, further comprising the step of guiding said flexible dose administrator so as to not enter an opening to a false nostril.
189. An equine intranasal delivery device as described in claim 188, wherein said dose comprises a substance selected from the group consisting of: a composition, a therapeutic composition, a prophylactic composition, a drug, a protein, a nucleic acid, an immunogen, an immunogen which elicits an immune response, a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26°C to about 30°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39°C, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39°C, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624), MSV+5 (identified by accession No.2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live

virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.

190. An intranasal delivery device, comprising:
- b. an intranasal probe coupled to said dose administrator;
  - a. a flexible dose administrator;
  - 5 c. an intranasal probe coupler having a first end responsive to said intranasal probe and a second end responsive to said dose administrator, wherein said intranasal probe coupler has at least one aperture which communicates between said volume of said dose administrator and an exterior surface of said intranasal probe;
  - 10 d. a force application element coupled to said dose administrator;
  - e. a coupler element having a first end responsive to said dose administrator and a second end responsive to said force application element, wherein said coupler element has at least one aperture which communicates between a volume of said dose administrator and said force application element;
  - 15 f. a dose-location coordinate indicator responsive to said flexible dose administrator; and
  - g. a dose;
191. An intranasal delivery device as described in claim 190, further comprising a force dissemination contact surface having hebetated termini responsive to said exterior
- 20 surface of said intranasal probe.
192. An intranasal delivery device as described in claim 191, further comprising a fluid dose propellant which separates said dose from said force application element.
193. An intranasal delivery device as described in claim 192, further comprising a conformable dose sequestration element having a sequestration volume sufficient to
- 25 sequester said dose, wherein said sequestration volume communicates with said dose delivery aperture element and said fluid dose propellant.
184. An intranasal delivery device as described in claim 193, wherein said fluid dose

propellent has a greater volume than a minimum dose delivery volume.

195. An intranasal delivery device as described in claim 194, wherein said conformable dose sequestration element further comprises a dose retainer, wherein said dose retainer positions said dose proximate to said dose delivery aperture.
- 5 196. An intranasal delivery device as described in claim 195, further comprising a stream delivery element coupled to said dose delivery aperture.
- 10 197. An intranasal delivery device as described in claim 196, wherein said dose comprises a substance selected from the group consisting of: a composition, a therapeutic composition, a prophylactic composition, a drug, an immunogen, an immunogen which elicits an immune response, a protein, a nucleic acid, a live virus, or a reassortant live virus.
198. An equine intranasal delivery device as described in claim 197, wherein said dose-location coordinate indicator has a position which assures a dose-location coordinate temperature between about 26° C to about 34° C.
- 15 199. An intranasal delivery device as described in claim 198, wherein said dose comprises a substance selected from the group consisting of: a live virus, a reassortant live virus, a cold-adapted live virus, an attenuated live virus, an equine cold-adapted live influenza virus which replicates in embryonated chicken eggs within a temperature range from about 26°C to about 30°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 37°C, an equine influenza cold-adapted live virus which does not form plaques in tissue culture cells at a temperature above about 39°C, a equine cold-adapted live virus having a phenotype wherein protein synthesis is inhibited above about 39°C, an equine cold-adapted live virus having a dominant interference phenotype, an equine influenza cold-adapted live virus derived from strain A/equine/ Kentucky/1/91 (H3N8), EIV-P821(identified by accession No. ATCC VR 2625), EIV-P824 (identified by accession No. ATCC VR 2624),
- 20
- 25

MSV+5(identified by accession No. 2627), any progeny of any of said equine influenza viruses identified by such accession Nos., any EIV having the identifying characteristics of said ATCC VR strains, or an equine influenza cold adapted live virus having about  $10^5$  TCID<sub>50</sub> to about  $10^8$  TCID<sub>50</sub> units.

5 200. An intranasal delivery device as described in claim 199, further comprising a dose diluent, wherein said dose and said dose diluent are combined.

201. Methods substantially as described hereinbefore and with reference to any of the accompanying examples.

10 202. Apparatuses substantially as described hereinbefore and with reference to any of the accompanying examples.

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## VII. ABSTRACT

This invention relates to apparatus and methods of delivering various compositions including medicaments to a variety of targets. The invention includes a dose administrator (1) which may be used for intranasal delivery of compositions or medicaments, such as live virus vaccines, to both humans and animals. An axial collapse prevention element (2) to prevent excessive axial deflection of the dose administrator (1) or a dose-location coordinate indicator (3) to facilitate the delivery of a dose to the desired target location may be coupled to the dose administrator (1). An intranasal probe (4) having a force dissemination contact surface (7) may be responsive to a first end of the dose administrator (1). The dose may be delivered from a conformable dose sequestration element (10) through an aperture which penetrates the dose delivery aperture element (5) and the dose may be caused to stream by coupling a stream delivery element (6) to the dose delivery aperture element (5). The force application element (12) which acts upon the dose may be separated from the dose by a fluid dose propellant (13). While the invention may be used for numerous applications, it specifically addresses the difficulties of delivering cold-adapted live equine influenza viruses intranasally to equids.



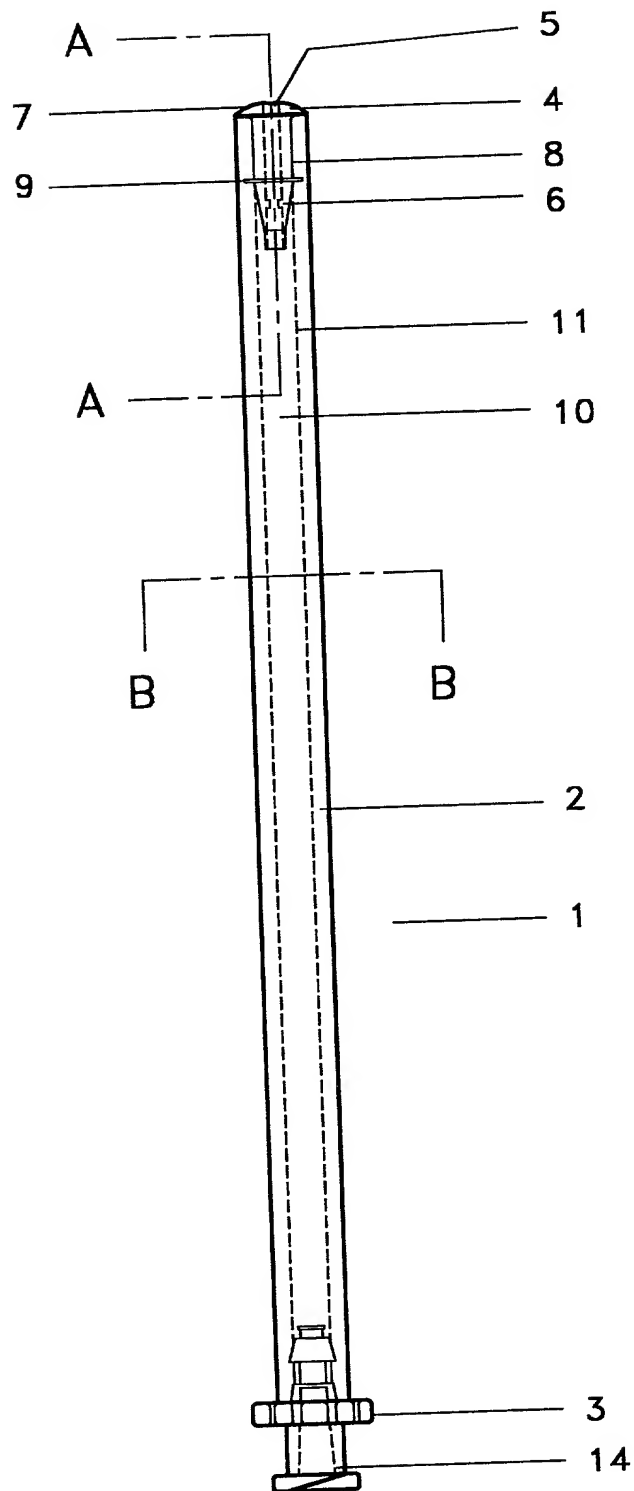


Fig. 1

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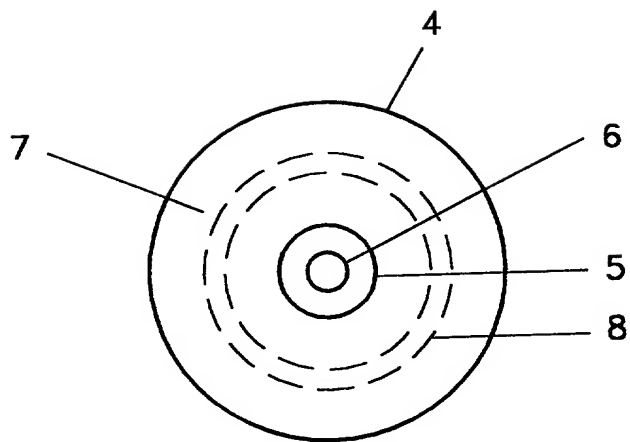


Fig. 2

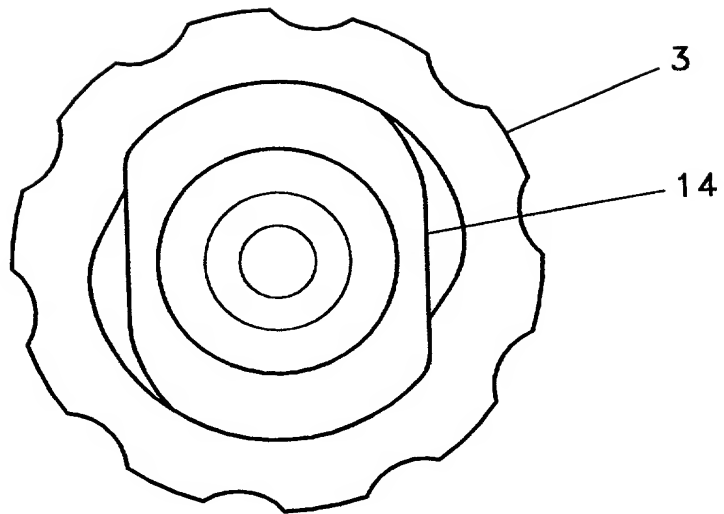
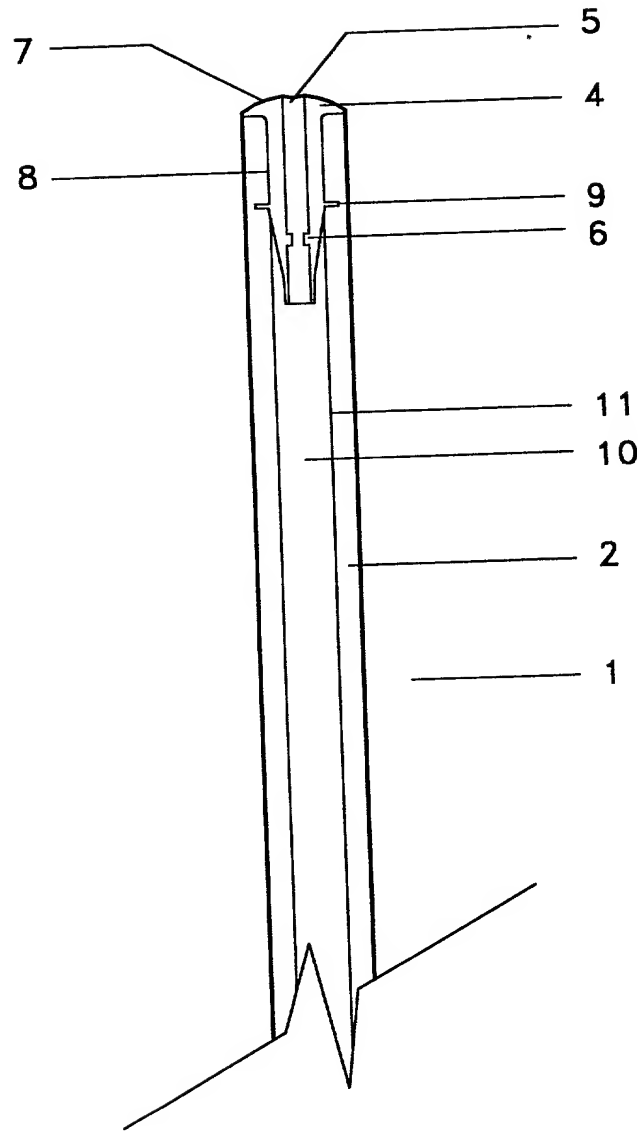


Fig. 3

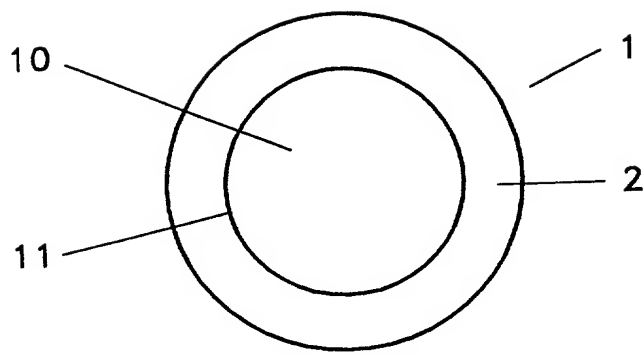
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Section A-A

Fig. 4

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Section B-B

Fig. 5

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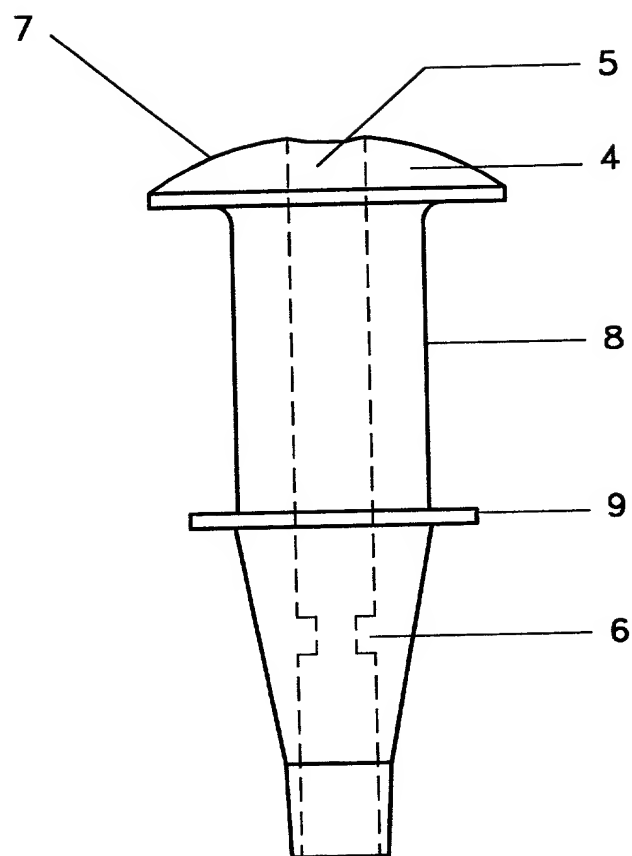


Fig. 6

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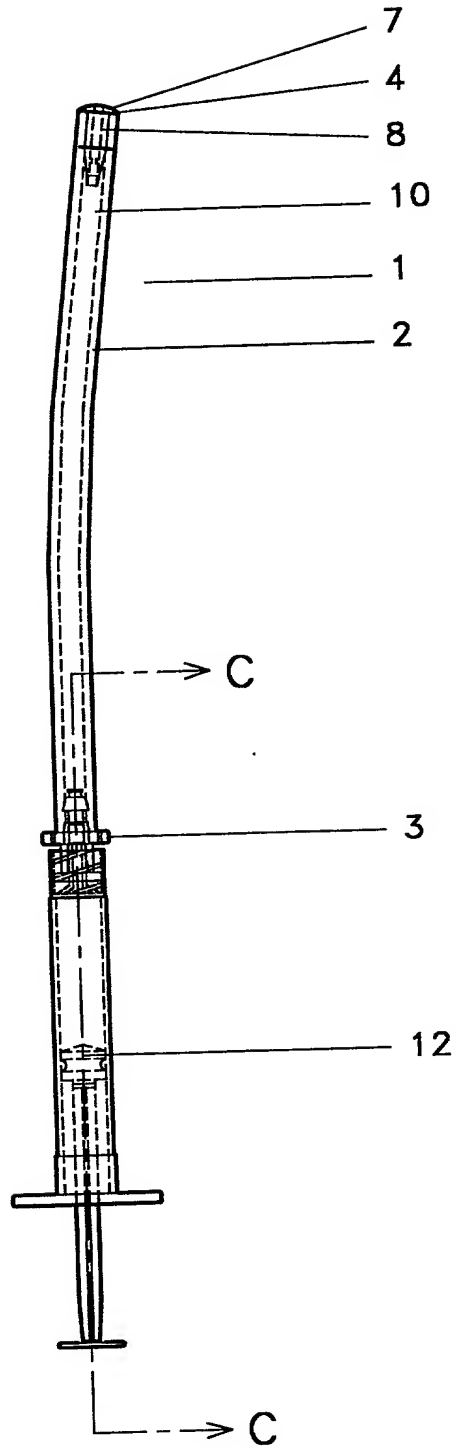
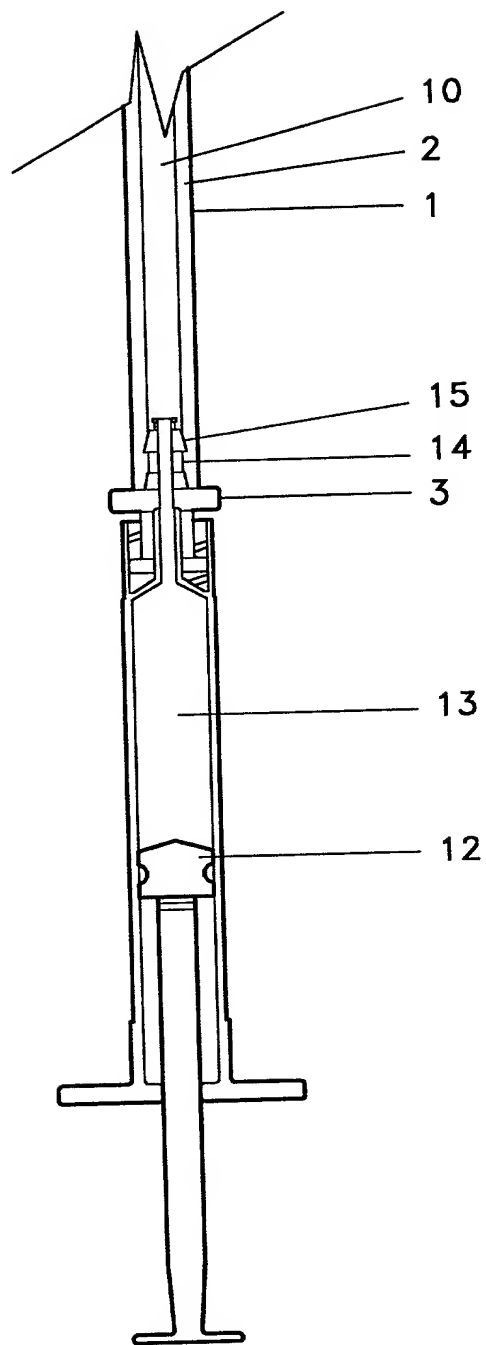


Fig. 7

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Section C-C

Fig. 8



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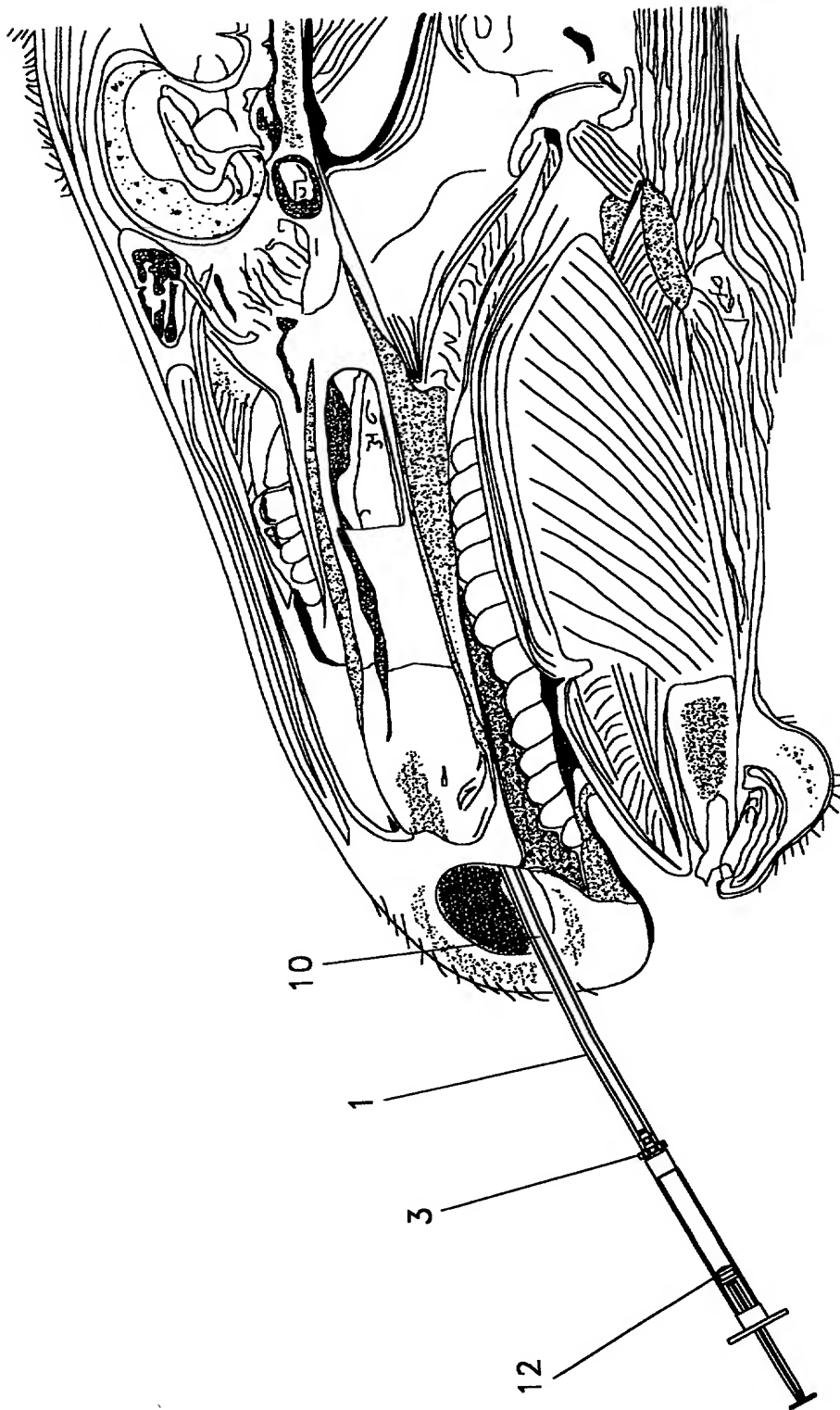


Fig. 9

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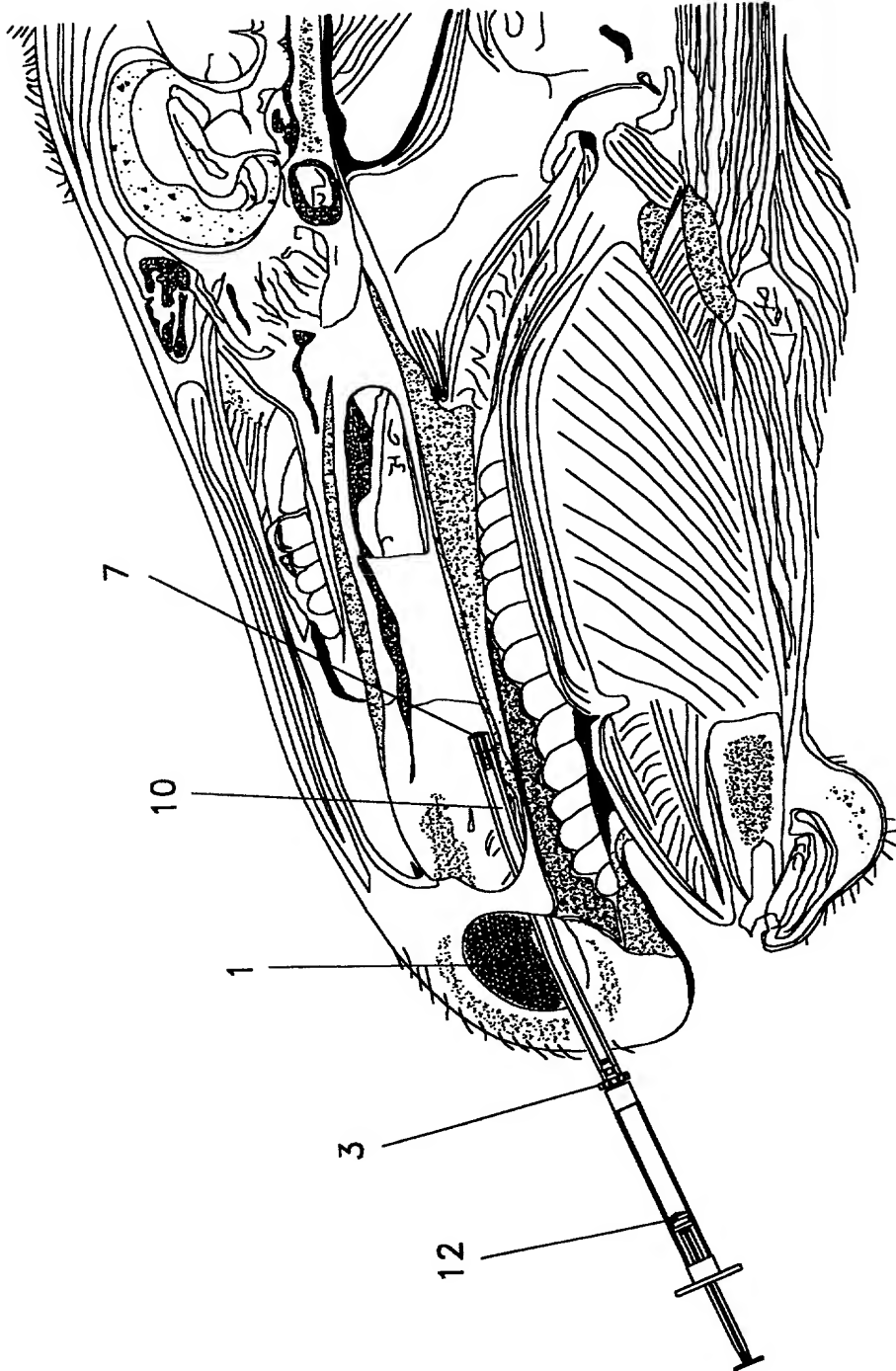


Fig. 10

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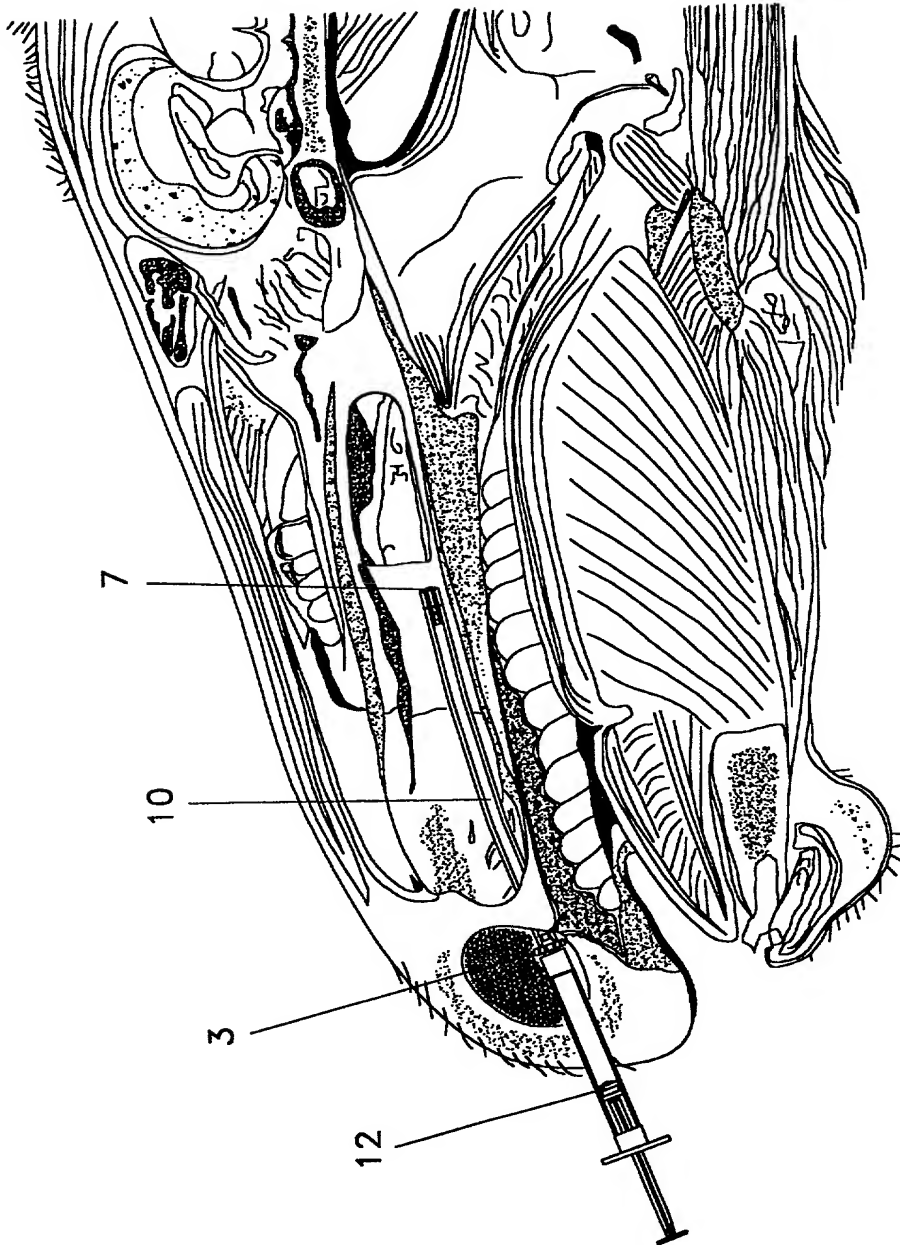


Fig. 11

IN THE UNITED STATES PATENT  
AND TRADEMARK OFFICE

In Re the National Phase Application of: Heska Corporation

Serial Number: (original) US 09/408,584 New: \_\_\_\_\_  
(PCT) PCT/US00/26870

Filed: (original US) 29 September 1999 New: \_\_\_\_\_  
(PCT) 29 September 2000

For: Intranasal Delivery System

POWER OF ATTORNEY

I, James H. Fuller, President and Chief Operating Officer, Heska Corporation, hereby appoint Santangelo Law Offices, P.C., whose mailing address is 125 South Howes, Third Floor, Fort Collins, Colorado 80521, including Luke Santangelo, whose registration number before the United States Patent and Trademark Office is 31,997, Craig R. Miles, whose registration number before the United States Patent and Trademark Office is 45,954, and Alfred K. Wiedmann Jr., whose registration number before the United States Patent and Trademark Office is 48,033 as Heska Corporation's attorney(s)/agent(s) to prosecute this application entitled "Intranasal Delivery System" and to transact all business in the Patent Office connected therewith. The undersigned acknowledges that the agent(s) appointed are attorneys for the assignee, Heska Corporation, only.

Dated this 21<sup>st</sup> day of March, 2002.

By: James H. Fuller  
James H. Fuller  
President and Chief Operating Officer  
Heska Corporation

IN THE UNITED STATES PATENT  
AND TRADEMARK OFFICE

In Re the National Phase Application of: Heska Corporation

Serial Number: (original) US 09/408,584 New: \_\_\_\_\_  
(PCT) PCT/US00/26870

Filed: (original US) 29 September 1999 New: \_\_\_\_\_  
(PCT) 29 September 2000

For: Intranasal Delivery System

DECLARATION FOR PATENT APPLICATION

This Declaration is made by Steven J. Penner and Randal W. Sebring.

I, Steven J. Penner, hereby declare:

- I am a citizen of the United States of America and that my residence and mailing address is: 924 East 6<sup>th</sup> Avenue, Broomfield, CO 80020.

I, Randal W. Sebring, hereby declare:

- I am a citizen of the United States of America and that my residence and mailing address is: 2706 Stockbury Drive, Fort Collins, CO 80525.

We believe that we are the original, first, and joint inventors of the subject matter which is claimed and for which a patent is sought on the invention entitled "Intranasal Delivery System;" and:

- United States Application Number 09/408,484 filed September 29, 1999 (the "Original US Application") originally entitled "Intranasal Delivery System", and
- PCT Application Number PCT/US00/26870, filed on September 29, 2000, entitled "Intranasal Delivery System" designating the United States of America;

the specification(s) of which have been provided to us at or prior to the time of signing this declaration, and of which we hereby claim the benefit and priority pursuant to 35 U.S.C §§119, 120, or 365; there are no foreign applications having a filing date before that of the application(s) on

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which priority is claimed; and, if applicable, we have identified in the request of this application, in compliance with PCT Rule 4.10, any claim to foreign priority and we have identified above by application number, country or Member of the World Trade Organization, day, month and year of filing, any application for a patent or inventor's certificate filed in a country other than the United States of America, including any PCT international application designating at least one country other than the United States of America, having a filing date before that of the application on which foreign priority is claimed.

We acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56(a). Further, insofar as the subject matter of any claims of this application was not disclosed in the prior United States or PCT International application we acknowledge the duty to disclose information which is known to be material to patentability as defined in Title 37, Code of Federal Regulations 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

We hereby grant the firm of Santangelo Law Offices, P.C., the power to insert on this Declaration any further identification which may be necessary or desirable in order to comply with the rules of the United States Patent Office or any foreign patent office including but not limited to inserting the application number, or the filing date of the above-entitled United States Patent Application based upon the Invention.

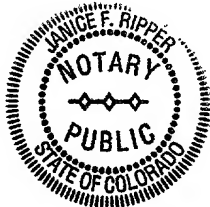
Date: March 4, 2002

Steven J. Penner  
Steven J. Penner

UNITED STATES OF AMERICA )  
STATE OF COLORADO )  
COUNTY OF BOULDER )

SUBSCRIBED AND AFFIRMED OR SWORN to before me in the County of BOULDER, State of Colorado, United States of America by Steven J. Penner, on this 4<sup>th</sup> day of MARCH, 2002.

WITNESS my hand and official seal pursuant to the authority vested in me as a Notary Public by the State of Colorado.



Notary Public Janice F. Ripper  
Address: 5370 MANHATTAN CIRCLE  
BOULDER, CO 80303  
My Commission Expires: NOV. 22, 2003

Date: 3-21-02

Randal W. Sebring  
Randal W. Sebring

UNITED STATES OF AMERICA )  
STATE OF COLORADO )  
COUNTY OF LARIMER )

SUBSCRIBED AND AFFIRMED OR SWORN to before me in the County of LARIMER, State of Colorado, United States of America by Randal W. Sebring, on this 21<sup>st</sup> day of MARCH, 2002.

WITNESS my hand and official seal pursuant to the authority vested in me as a Notary Public by the State of Colorado.

Notary Public Susan A. Gordon  
Address: 342 Sunmountain Dr.  
Loveland, CO 80538  
My Commission Expires: Nov. 22, 2004

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